Chemosurgery
in
Cancer, Gangrene and Infections

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FEATURING A NEW METHOD FOR THE MICROSCOPICALLY CONTROLLED EXCISION OF CANCER

By

FREDERIC E. MOHS, B.Sc., M.D.

Associate Professor of Chemosurgery Department of Surgery
University of Wisconsin Medical School
Head of the Chemosurgery Clinic
State of Wisconsin General Hospital
Research Associate McArdle Memorial Laboratory for Cancer Research
Madison Wisconsin



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Preface

During the twenty years the author has devoted to the development and clinical evaluation of the chemosurgical treatment of cancer, a considerable body of information concerning this new method has been accumulated. Only a part of this data has been included in the published articles and these are scattered throughout various scientific periodicals. It was felt, therefore, that there was a need for a comprehensive volume on the development and the various clinical uses of chemosurgery.

Much of the book relates to the role of chemosurgery in the treatment of cancer since this is the chief use of the method. The general features of the technic by which the all-important microscopic control of excision is accomplished is described in the chapter on technic. More specific technical details are included in subsequent chapters on cancer in various locations including the face, nose, ear, eyelids, extremities and trunk, lips, mouth, sinuses, larynx, salivary glands, breast, penis and scrotum, vulva, vagina and cervix, anus and lower rectum, and metastatic carcinoma in the lymph nodes. This subdivision according to anatomic site also facilitates the presentation of the descriptive, pictorial and statistical material upon which the results of treatment may be evaluated. The special problems of melanoma, sarcoma and endothelioma also are considered.

In addition there is a chapter on the modes of spread of external cancer, a subject which could be studied adequately only by means of the microscopic visualization afforded by the chemosurgical technic. This study brings out the fact that cancers often send out extensions which are clinically undetectable. It is the frequent occurrence of these "silent" extensions that accounts for the increased reliability and the increased conservatism attainable with the microscopically guided excisions which characterize the chemosurgical treatment of cancer.

Some benign tumors are amenable to chemosurgical treatment and, although the microscopic control is not as important as it is in the treatment of cancer, it often is helpful in determining if the tumor actually is benign and in deciding how extensive the excision should be. Among the benign tumors are included epithelial tumors, connective tissue tumors, hemangiomas, pigmented nevi, tumors of infectious origin and precancerous lesions.

Chemosurgical removal of gangrenous parts often can be accomplished at a more conservative level than would be consistent with healing following ordinary surgical amputation. Here the microscopic control is not required because gross visualization is adequate. The primary use in this field is in the conservative amputation of the gangrenous digits which may occur in patients with diabetes, arterio-

sclerosis, frostbite and other conditions which produce vascular occlusion. However the technic also is useful in the treatment of decubitus ulcers and other necrotizing processes.

There are a number of infections which may be treated advantageously by chemosurgical removal In some conditions such as blastomycosis, actinomycosis and tuberculosis of the skin or deeper structures the microscopic control may occasionally be helpful, but in most of the considerable variety of infections which are amenable to chemosurgical treatment the progress may be followed by gross visualization

Treatment by means of surgery, electrosurgery, roentgen rays and radium have their place in certain lesions which may come to the attention of the chemosurgeon and, though these methods of treatment are not the primary subject of this book, their use in these conditions, either alone or in conjunction with chemosurgery are discussed This is in accord with my belief that chemosurgery is most advantageously practiced in large general hospitals where there may be free cooperation between the numerous specialists who are concerned with the treatment of cancer in its many forms.

It is hoped that this treatise will be helpful to the surgeons, dermatologists, radiologists, pathologists, otolaryngologists and other specialists concerned with the treatment of cancer Also it is hoped that this book will be of interest to general practitioners and others who have the responsibility of obtaining the most effective treatment for their patients suffering from cancer Moreover some of the technics described should be useful in the average physician s office examples are the simple methods described for the treatment of precancerous keratoses, leukoplakia, nevi, molluscum contagiosum granuloma pyogenicum, warts, plantar warts, hemangiomas, spider nevi, gangrene, and pilonidal sinus.

The suggestions regarding the setting up of clinical and microtechnical facilities for the practice of chemosurgery should be of particular interest to those who elect to specialize, partly or completely in this new field.

Acknowledgments

To give full credit to the numerous individuals who have in some way contributed to the development of the chemosurgical method, would require a voluminous chapter. One would have to begin with the ancient Egyptian who first conceived the idea of killing cancer tissue with chemicals—in that instance with arsenic. Then one would mention Sir Humphry Davy who two hundred years ago discovered zinc chloride and first observed its caustic action on tissues. Some fifty years later such European workers as Canquoin of France and Bougard of Belgium extensively investigated the use of this chemical for the treatment of patients with accessible cancers. Then during the next century and a half the know how of chemical cauterization was transmitted through a relatively few physicians and through a host of irregular practitioners. Acknowledgment also would have to be made of the contributions of the many surgeons and other scientists who developed the various surgical instruments and technics which play an essential part in chemosurgical treatment. Finally one would give credit to the inventors of the microscope, the tissue stains, the freezing microtome and the other equipment, materials and methods which were essential to the development of the special microtechnical procedures which play an important part in the chemosurgical technic. Thus, chemosurgery with its three essential component parts—chemical treatment, surgical excision and microscopic examination—is the result of the synthesis of three kinds of know how produced by so many individuals that most of them cannot even be mentioned.

More specific acknowledgment may be accorded the men at the University of Wisconsin who played a more direct part in the various phases of the development and clinical application of the chemosurgical method. Dr Walter S Sullivan and Dr Harland W Mossman of the Department of Anatomy gave valuable suggestions regarding animal experiments and microtechnical procedures. Dr Michael F Guyer,* then Chairman of the Department of Zoology, collaborated in the animal experiments that led to the development of the chemosurgical technic, furthermore, he has maintained a constructive interest in the clinical applications and in the writing of this book.

Dr William S Middleton then Dean of the Medical School, guided the development of facilities for the clinical application of the chemosurgical method. Dr Robin C. Buerki former Superintendent of Wisconsin General Hospital aided in establishment of the first chemosurgical clinic. Dr William S Stovall, while Acting Superintendent arranged for the second clinic. Finally, Dr Harold M Coon present Superintendent of the University Hospitals, helped in the design of the present clinic in the new wing known as the Cancer Hospital. Both Dr Stovall

and Dr Walter H Jaeschke of the Department of Clinical Pathology have routinely examined the paraffin sections from each case and they often have given valuable assistance in the diagnosis of unusual types of lesions. The late Dr Roscoe L. McIntosh and Dr Otto H. Foerster of the Department of Dermatology were helpful in the early operation of the first chemosurgical clinic and in the delineation of the dermatologic indications. Dr Sture A. M Johnson and Dr Garrett A. Cooper have maintained a cooperative atmosphere between the Department of Dermatology and the Chemosurgery Clinic.

Dr Erwin R. Schmidt, Chief of the Department of Surgery early recognized chemosurgery as a significant addition to the surgical armamentarium against cancer, gangrene, and certain infections.[83] Hence, he provided a place for the Chemosurgery Clinic in the framework of the Department of Surgery In cases in which surgical care was required in addition to chemosurgical treatment, ready collaboration was constantly available not only from Dr Schmidt but also from Dr Kenneth E Lemmer, Dr Anthony R. Curreri, Dr Joseph W Gale and other members of the surgical staff In cases in which plastic repair was required, the skill of Dr Volney B Hyslop and, more recently, of Dr Wayne B Slaughter and Dr Frank D Bernard has been available Gynecologic consultation frequently was obtained from Dr Ralph E. Campbell and other members of the gynecologic staff Diabetic patients and others requiring special medical care were attended by Dr Elmer L. Severinghaus, Dr Edgar S Gordon and Dr Edwin C Albright as well as by Dr William S Middleton, Dr Ovid O Meyer and other members of the medical staff

A number of medical students have served as research assistants and each has made some contribution to the development of the chemosurgical method Dr Norman A. Franken helped to devise the microtechnical procedures by which frozen sections of large size could be cut, stained and mounted. Dr Erland O Otterholt, Dr Eugene J Nordby and others have helped to develop certain details of the chemosurgical technic and to compile the data needed for evaluation. Dr Theodore G Lathrop's doctorate thesis[41] concerned the patterns of spread of neoplasms as demonstrated by the chemosurgical technic while Dr Allan W Limberg's thesis concerned the indications for chemosurgical treatment.[42] Dr Franklin N Dukersheim's thesis[23] was concerned with the conservative treatment of peripheral gangrene with special reference to chemosurgical amputation Dr B M Kramer's thesis[49] was a survey of current methods of treatment of carcinoma of the skin

Some of the men who have come to visit or to receive training in the Chemosurgery Clinic have suggested ideas for the improvement of the chemosurgical technic. Notable among these was the suggestion by Dr Ray R Allington[7] that dichloracetic acid be used to control the capillary bleeding after the removal of the main mass of the neoplasm by curettage. Prior to that suggestion preliminary excision or curettage had been carried out only occasionally because the time gained by the procedure usually did not counterbalance the time lost securing hemostasis. Now the rapid control of capillary oozing makes possible the removal of the main mass in a few minutes therefore, this procedure now is carried out in the majority of the cases.

Among the other trainees and visitors who have contributed in some way to the development and propagation of chemosurgery are Dr Michael B Shimkin, Dr Herbert L. Traenkle,[illegible][illegible] Dr Wilbert Sachs,[illegible] Dr Herman E. Dustin, Dr Owen Millar, Dr Wayne Wong, Dr Gordon H Eckblad,[illegible] Dr Henry A. Szujewski,[illegible] Dr Richard Shepard,[illegible] Dr Jean Delacretaz, Dr Leon J H van Lierde,[104] Dr Gilbert A Beirne, Dr Ian B McDonald, Dr Theodore G Lathrop, Dr Eustaquio D Montero Dr Roger F Laubenheimer, Dr Thomas B Fitzpatrick, Dr C. Thomas Flotte and Dr Alcides L. Conti

Much credit is due those who arranged for the financial support of the experimental and clinical investigations that led to the development of the chemosurgical method. Thomas E Brittingham supported the research assistantship which I held under Professor M F Guyer when the idea of microscopically controlled excision of cancer had its inception His continued generous support during the subsequent laboratory and clinical investigations contributed greatly toward the successful outcome of the project. The Jonathan Bowman Memorial Fund supported the fellowship which I held while carrying out the final laboratory research and the early clinical trial of the method. The late Garnett W McKee provided funds for clinical facilities. The Wisconsin Alumni Research Foundation and more particularly its first director the late Dean Harry L. Russell, provided valuable counsel and financial support. The latter was in the form of research assistantships which were administered by President Edwin B Fred, who then was Dean of the Graduate School, and by his successor, Dean Conrad A. Elvehjem.

Over the years many assistants, technicians, nurses and secretaries have contributed not only to the steady improvement of the various details of the chemosurgical technic but also to the laborious acquisition and compilation of the statistical data and other material needed in the writing of this book. None have been more effective than the present staff which includes Robert Patnaude, assistant and technician Mrs. Eleanore Sweitzer, technician and nurse, Mrs. Rachel Caruso nurse, and Mrs. Esther Luedtke, secretary The photographs used in this book largely are the result of the skill of Homer Montague and his staff

For expert guidance and effective cooperation in the preparation of this book I am indebted to the publisher Charles C Thomas.

F E M

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CHAPTER 1

Experimental Background

THE new and most important feature of the chemosurgical method for the treatment of cancer is the technic by which complete microscopic control of excision is made practical. This technic was not suddenly envisioned in its entirety but it was gradually evolved by means of animal experiments conducted over a period of several years.

Origin of the Idea of Microscopically Controlled Excision

The idea that complete microscopic guidance of excision might be feasible was conceived in 1932 when, as a sophomore medical student I was working as a research assistant to Dr M. F. Guyer in the Zoology Department of the University of Wisconsin.[83] In an attempt to compare inflammatory reactions in cancer tissues with those in normal tissues, we were injecting various irritants into transplantable cancers and into normal tissues of rats. One of the injected irritants was a 20 per cent solution of zinc chloride. This concentration, inadvertently was too strong and instead of merely producing an inflammation it produced necrosis at the site of injection. Nevertheless, the tissues were removed several days after the injection and microscopic sections were made. Upon examination of the sections we were interested to observe the excellent preservation of the microscopic features of the tissues which had been killed by the zinc chloride. Obviously the chemical had acted as an in situ fixative and th fixation was much the same as if the tissue had been excised and fixed in vitro.

In itself the observation of fixation in situ was of no particular significance. However the observation was important in that it initiated a train of thought which led, several years later to a method by which cancer could be excised under complete microscopic control.

At first, the exact means by which microscopic control might be attained was not apparent. Experiments with representative biopsies from scattered areas suspected of being cancerous offered little promise of reliability because foci of cancer between the biopsies readily could be overlooked. Attempts to overcome this deficiency included the use of serial sections of excised specimens, but this procedure proved impractical because of the large number of sections required.

Finally the idea was conceived of dividing the entire excised layer of fixed tissue into specimens of convenient size and then cutting frozen sections through the under surface of each flat specimen. This innovation made practical the thorough systematic microscopic examination of the entire area suspected of containing cancer. Later refinements of the technic made orientation so exact that the most minute areas of cancer could be precisely located with the result that the finest ramifications of a neoplasm could be followed out and destroyed in a highly selective manner.

Definition of Chemosurgery

The term "chemosurgery" was coined to indicate that the tissues are chemically treated and then surgically excised. Unfortunately the term does not mention the most important feature of the method, the microscopic control. However it was felt that a more inclusive term such as chemicrosurgery would be too cumbersome. Furthermore, while such a term would accurately designate the method as applied to the treatment of cancer it would not appropriately apply to the chemosurgical pro-

cedures used in the treatment of gangrene and infections because in these conditions microscopic control of excision is not necessary.

Nevertheless the term, chemosurgery, when used to denote the method as used in the treatment of cancer definitely should connote microscopically controlled excision. Therefore, a dictionary definition of chemosurgery might be as follows:

chemosurgery (kĕm-o-ser jer-e) the removal of tissue such as malignant, gangrenous or infected tissue, after it has been fixed by chemical means. In the treatment of external cancer the purpose of the chemical fixation in situ is to facilitate the systematic microscopic control of excision through the use of frozen sections.[illegible]

Chemicals for Fixation in Situ

A number of chemicals, other than zinc chloride, were tested not only for their ability to produce satisfactory fixation of the microscopic structures of the tissues but also for toxicity, ability to diffuse into the tissues, controllability of the depth of penetration and other characteristics.

Some chemicals, such as the caustic alkalies, produced excessive liquefaction with disruption of the gross and microscopic structure of the tissues. Arsenic trioxide, phenol, mercuric chloride and antimony trichloride produced adequate fixation but they were eliminated because they were too toxic to be used safely in the treatment of large cancers. Silver nitrate was unsuitable because of the danger of argyria. Some chemicals, such as formalin, had objectionable odors.

The most satisfactory fixative from every standpoint was zinc chloride, a chemical first extensively used for the destruction of cancer over a century ago by Canquoin [7] of Paris and Bougard[13] of Brussels. This substance in a proper base produced adequate fixation, penetrated well, was thoroughly controllable, produced no appreciable systemic toxicity, was odorless, and was safe to handle since it had relatively little effect on the intact skin. Moreover, zinc chloride did not adversely affect the reactivity or the healing qualities of the tissues just beyond the deepest level of fixation. To this quality of the chemical is credited not only the rapid separation of the final layer of fixed tissue but also the healthy nature of the granulation tissue, the rapid epithelization and the minimal scarring which follows its use. Tissues destroyed by heat, by contrast, are slow to slough, the granulations are less healthy and more subject to infection, epithelization is less prompt and scarring often is excessive. There is evidence that these adverse effects of heat are due to the thermal damage of the tissues just beyond the deepest level of cauterization.

Vehicles for Fixative Chemicals

Early in the animal experiments it became evident that the injection of fixative chemicals was an unsuitable means of administration. In the first place, it was not possible to deposit the injected solution accurately because of the tendency for the material to permeate irregularly along various tissue planes with the result that fixation was erratic. In the second place, not infrequently the solution inadvertently was injected into blood vessels with resultant convulsions and death of the rats, often within two minutes.

The application of fixative solutions or of gauze soaked in fixative solutions also was unsuitable because of insufficient and erratic penetration.

The best mode of administration was by means of a paste type of vehicle. For accurate control of fixation over a wide range of depths it was found essential that the base have two special characteristics: first, low affinity for the fixative solution, and, second, high permeability. The low affinity of the vehicle for the fixative served to permit the ready exit of the chemical from the paste in favor of the tissues to which it was applied, whereas the high permeability of the vehicle facilitated the permeation of the fixative from all levels of the applied paste regardless of the thickness of application. The latter quality made it possible to vary penetration from a depth of less than 1 mm. to more than 1 cm. in twenty-four hours by simply altering the depth and area of application.

Both the low affinity and the high permeability were attained by the use of certain finely granular insoluble substances as the predominant constituents of the vehicle. These substances were called "permeants" because the

multiple interfaces between the particles produced a highly permeable matrix These granules also had a low affinity for the fixative solution with the result that the chemical would readily leave the paste in favor of the tissues to which it was applied Some of the permeants used were stibnite pyrolusite limonite, hematite, and clinkers from bituminous coal. The essential characteristics of the permeants were as follows (1) Granularity but with no granules larger than would pass through an 80 mesh sieve Larger particles resulted in gritty pastes which were difficult to apply accurately Too large a proportion of very fine particles produced soft painty" pastes which tended to "creep" out of position and which left residues which were difficult to wash off (2) Specific gravity of 4 or more. The heavier the materials which composed the paste the less was the chance of displacement after application. (3) Insolubility in and nonreactivity with the fixative solution. (4) Dark color preferably black, to contrast with the tissues and blood

A small amount of an "agglutinant" was necessary to bind the particles of permeant together Without an agglutinant the paste had such a crumbly consistency that it was difficult to apply Moreover when the agglutinant was omitted the fixative solution tended to settle to the bottom of the container upon standing Agglutinants were any of a variety of plant extracts such as Sanguinaria canadensis Phytolacca decandra, Podophyllum peltatum or Inula helenium. More common agglutinants such as starch and wheat flour were somewhat inferior but rye flour was fairly satisfactory

To the thoroughly mixed permeant and agglutinant substances the fixative chemical was added as a saturated solution. Zinc chloride made up 40–50 per cent of the preparation by weight. A satisfactory preparation was the following

Stibnite (80 mesh sieve)	40 0 gm.
Sanguinaria canadensis	10 0 gm.
Zinc chloride, saturated solution	34 5 cc

In this preparation (Z-108a) zinc chloride made up approximately 45 per cent of the weight. This formula with slight modification in the amount of zinc chloride solution occasioned by different batches of stibnite has been in constant use since 1937 * It has provided thoroughly predictable penetration in the hands of operators familiar with the various factors which affect penetration These factors which were studied by means of both animal and clinical experiments, are discussed in the chapter on technic.

Histology of Tissues Fixed in Situ

The effects of the various fixative chemicals on the histology of tissues were determined by their application to cancers in rats The applied fixative preparations were held in place by means of cotton dressings which were affixed by adhesive strips sutured in place to prevent loosening by the claws or teeth. The sections were made by the usual freezing or paraffin imbedding technics followed by hematoxylin and eosin staining

Except for the strong acids and alkalies, all of the tested chemicals produced fixation which was good enough for easy diagnosis after one became acquainted with the alterations in tissue structure produced by each fixative.

The dehydrating effect of zinc chloride caused some shrinkage of the cells with resultant increased density of the cytoplasm pyknosis and increased basophilism of the nuclei and the formation of clefts between the cells (Fig 54C) However with experience the histologic structure of the tissues could be recognized easily Antimony chloride caused the nuclei to become swollen and vesicular and, with too strong action, produced an amorphous basophilic mass useless for diagnosis Phenol produced moderate shrinkage and distortion Mercuric chloride and silver nitrate produced excellent fixation. In general the chemicals

* The prepared fixative paste may be obtained from the School of Pharmacy University of Wisconsin, Madison Wisconsin. Currently the best source of stibnite is the Hummel Chemical Company Inc., 90 West Street, New York 6 New York. With material from this source the formula is altered as follows. Stibnite 40 0 gm Sanguinaria canadensis, 3.25 gm and zinc chloride, saturated solution, 24 2 c.c. Sanguinaria canadensis may be obtained from S B Penick and Company 50 Church Street New York 8 New York or 735 West Division Street, Chicago 10 Illinois.

which formed proteinates of heavy metals produced the best fixation.

Twenty-four hours after the application of a fixative such as zinc chloride to normal tissues there developed a leukocytic infiltration at the junction between the fixed and unfixed tissues. By forty-eight hours this formed a well defined wall of leukocytes in which dissolution of the tissues began to occur. This process culminated in the separation of the fixed tissue after six or seven days.

For some unknown reason there was practically no leukocytic infiltration at the junction between the fixed and unfixed cancer tissue. However this lack of inflammatory reaction in cancer tissue did not appreciably reduce the rate of separation of the fixed tissues. Incidentally this lack of leukocytic infiltration of cancer tissue during chemosurgical treatment has proved to be an advantageous phenomenon because, even though the surrounding normal tissues may be obscured by dense masses of leukocytes, the cancer remains uninfiltrated and readily recognizable under the microscope.

Effect of Fixation in Situ on Metastasis

To determine if the reactions set up in cancer tissue by treatment with fixative chemicals might increase the tendency for metastasis to occur repeated subcurative doses of zinc chloride were applied to transplantable carcinomas in rats. Flexner Jobling carcinomas ranging in size from 2 to 4.5 cm. in diameter were paired off in equal sizes in the treated and control groups. In four experiments the treated tumors were injected with 0.1 cc. of an 8–25 per cent zinc chloride solution, while the controls were untreated except for one group which received physiological saline solution. In two other experiments treatment consisted of daily applications of a small amount of 40 per cent zinc chloride paste. Such subcurative doses were administered over a period of four to eight weeks. Rats dying during this period were examined for axillary pulmonary and mediastinal metastases as were the rats killed at the termination of the experiment.

The results of these experiments were consistent in all of the groups and may be summarized as follows. In the group of fifty-three control rats metastasis occurred in 41.5 per cent while in the group of sixty-one treated rats metastasis occurred in only 27.8 per cent. Thus, instead of an increase in metastasis there actually was a decrease despite the purposely prolonged use of subcurative, irritating doses of zinc chloride. The lower incidence of metastasis in the treated group was observed whether the spread was by the lymphatic route to the axilla or by the blood vascular route to the lungs and the mediastinum. Apparently the chemical inflammation produced by the zinc chloride reduced the permeability of the lymphatics and blood vessels in a manner similar to the protective reduction of vascular permeability which occurs in inflammation due to infection.

Since the purposely prolonged chemical irritation of cancer had no tendency to increase metastasis in rats it seemed extremely unlikely that the rapid chemical removal of cancer in man should accelerate metastasis. Subsequent clinical experience in the treatment of over 4000 patients with cancer has borne out this conclusion.

PART I

MALIGNANT TUMORS OF THE SKIN AND OTHER ACCESSIBLE STRUCTURES

CHAPTER 2

Chemosurgical Technic

THE microscopic control of excision which characterizes the chemosurgical method is accomplished by the employment of three essential procedures in the following sequence (1) chemical fixation, in situ of the tissues suspected of being neoplastic (2) excision of a layer of the fixed tissues, and (3) systematic microscopic examination of the excised layer as a guide to further treatment.

To attain complete microscopic control it is essential that this sequence be followed out in every case. However it is optional whether the grossly visible portion of the cancer be removed surgically or chemosurgically As originally described,[13] the chemosurgical method was used to remove the entire neoplasm but because of the saving of time and reduction of discomfort to the patient which often results from the preliminary surgical removal of the main mass of cancer the latter procedure now is carried out in most cases.

Preliminary Surgical Removal of the Main Mass of Cancer

If an appreciable mass of cancer obviously is present, and if the neoplasm is of a type which will not be disseminated by manipulation, the grossly visible or palpable portion may be removed under local anesthesia by the cold knife, the curet, the electrosurgical unit or a combination of these modalities.

If the lesion is large or located in an unusually sensitive area, preoperative medication may be desirable not only to reduce the discomfort from the injection of the local anesthetic but also to reduce the discomfort from the penetration of the fixative after the anesthetic has worn off The potency of the analgesic may range from that of aspirin to that of morphine Morphine sulfate, 1/6 grain (10 mg) or a combination of codeine phosphate 1/2 grain (30 mg) and aspirin 10 grains (0 6 gm.) usually suffice Equivalent proprietary preparations such as codempiral also are satisfactory

Local anesthesia is accomplished either by local infiltration or by regional block using a solution of procaine hydrochloride. The strength of this solution may vary from 1 to 2 per cent, but 1.5 per cent has been found most satisfactory because it has less tendency to damage the tissues than 2 per cent and it provides better anesthesia than lower concentrations. Usually the injections are quite painless if an epidermal wheal is made and a moment is allowed to elapse before the needle is plunged through the full thickness of the skin. Often both a block of the nerve supplying the area and local infiltration are employed for example in cases of cancer of the lip the mental nerve may be injected and then the lower lip infiltrated around the neoplasm. Great care must be exercised to avoid injecting too close to the neoplasm because passage of the needle through an outgrowth of cancer tissue could lead to implantation of malignant cells along the needle tract. Moreover the disruption and water logging of the tissues unnecessarily increase the difficulty of the removal and sectioning of the specimens. Rarely is a general anesthetic indicated but on occasion it may be useful if the neoplasm is so located that there is difficulty in producing adequate local anesthesia. Occasionally analgesia is obtained with nitrous oxide or trichloroethylene (Trimar)

The choice of the scalpel the curet or the electrosurgical instrument depends on the size location and pathologic diagnosis of the neoplasm. The scalpel and curet are used for most

lesions on the external surface but the electrosurgical unit is more commonly used for the larger lesions in the mouth where chemical hemostasis may be delayed by the diluting effect of the saliva. If there is any suspicion of melanoma surgical diathermy must be avoided because of the disseminating effect of the "tissue steam" produced by the heat generated during this procedure.

Usually the main mass of a cancer on an external surface is excised by means of a scalpel. The depth of the initial incision depends upon the clinically apparent depth of the neoplasm as indicated by visualization and palpation. The "feel" of the tissues as the knife passes through them also is helpful in determining the depth of the incision. The object is to remove the grossly discernible portion of the cancer leaving a saucerized surface from which to proceed with chemosurgical treatment. The excised tissue provides good specimens for frozen and paraffin sections. The technic is illustrated in Figure 58

After excision with the scalpel, the bleeding surface is wiped off quickly and the cut surface is inspected to determine whether any visible cancer remains. Wherever further neoplastic tissue is observed another layer may be excised. Nodular basal cell carcinomas and other cancers with scanty fibrous stroma often can be scraped out at this point with a curet. The usefulness of this instrument in conjunction with chemosurgery has been pointed out by R. R. Allington and his co-workers.[7] Ring curets from 3 to 8 mm. in diameter are used. Not infrequently the curet will sink into unsuspected pockets of soft friable neoplastic tissue which is readily distinguished from the normal tissue which cannot be curetted out unless much greater pressure is exerted. The grating sound and "feel" produced by the curet also are characteristic of normal tissues. Unfortunately the curet is ineffective when the neoplasm has a profuse fibrous stroma or when the neoplasm is associated with scarring from previous therapy Such tissue resists the curet as much as does normal tissue and it produces the same "grating sensation.

Following removal of the main mass of cancer by the scalpel or curet capillary oozing is controlled by the application of dichloracetic acid. To avoid excessive dilution, the acid-soaked applicator must follow as closely as possible behind the applicator or gauze which is used to wipe off the blood Larger bleeders require the application, under momentary pressure of small squares of gauze which have been impregnated with the zinc chloride fixative paste. Often bleeding is reduced by stretching the lesion over a prominence of bone or cartilage until the chemicals have produced hemostasis. If any cancer becomes visible after hemostasis another layer may be pared off of the involved area and hemostasis again secured. Dichloracetic acid then is applied to the skin at the periphery of the lesion to render the stratum corneum permeable to zinc chloride. Finally zinc chloride fixative paste is applied to produce fixation in preparation for the microscopically guided chemosurgical excisions which are carried out in a manner to be described presently

Excision of the main mass of cancer by means of a surgical diathermy instrument, such as the Bovie unit, may be indicated in cases in which bleeding otherwise might be troublesome. By this modality capillary oozing is prevented by the cutting current while bleeding from the larger vessels is controlled by the coagulating current. Unfortunately the cutting current and more particularly the coagulating current produce a certain amount of eschar which tends to retard the penetration of the fixative chemical. This results in irregular penetration with the least fixation occurring about the larger vessels which have been coagulated. Therefore there may be more bleeding than usual during the excision of the first layer of chemically fixed tissue. Moreover this first layer tends to be more soft and friable than usual with the result that the specimens are more difficult to handle during excision and more likely to break up during the preparation of the microscopic slides. A final disadvantageous feature of the electrosurgical instrument is that it, in common with all instruments which cut or destroy tissue by means of heat, has the tendency to produce tissue steam which disrupts the tissue and may disseminate certain neoplasms by the propulsion of emboli of

malignant tissue through the lymphatic or blood vessels. This undoubtedly would increase the chance of metastasis from neoplasms which tend to metastasize readily, as for example, melanoma. In point is the series of cases reported by Amadon,[*] in which metastasis occurred in every patient with melanoma treated by electrocoagulation Whether squamous cell carcinoma with a high grade of malignancy might be affected similarly is a possibility as yet incompletely explored It would seem extremely unlikely however that low grade squamous cell carcinoma or basal cell carcinoma would be spread by electrosurgical treatment.

There are fairly numerous occasions when preliminary surgical or electrosurgical excision is contraindicated A few examples are as follows (1) A cancer with such obscure outlines by gross examination that microscopic guidance from the beginning is necessary Some morphea like and rodent ulcer types of basal cell carcinomas fall into this category as do some cancers which have recurred in scars from previous radiation or surgical treatment. (2) A cancer which is so located that adequate local anesthesia is difficult to attain. (3) A deeply invasive cancer on a thin structure such as the ear or the nasal cartilage where there is some danger of penetration through the full thickness. In such cases the edema produced by the initial application of the fixative increases the thickness of the structure giving a greater factor of safety (4) A melanoma which is so prone to metastasize that neither surgical or electrosurgical excision of the main mass is safe. In such cases the entire neoplasm should be removed chemosurgically

Preparation of the Patient for Chemosurgery

If it is decided to begin chemosurgical treatment without prior surgical removal and if the lesion affects a large or especially sensitive area, preliminary analgesic medication is used to reduce the discomfort from the initial application of the keratolytic and fixative chemicals. Sometimes aspirin 10 grains (0 6 gm.) suffices, but frequently codeine demerol or morphine in appropriate doses are employed. A commonly used medication is morphine sulfate, 1/6 grain (10 mg)

If the lesion is located on mucous membranes preliminary medication with atropine 1/120 grain (0.5 mg) may also be used to reduce the secretions which may dilute the chemicals to a troublesome extent.

Application of the Keratolytic Chemical

Keratin forms a barrier to the passage of zinc chloride Therefore a keratolytic chemical such as dichloracetic* or trichloracetic acid is applied to render the stratum corneum permeable to the fixative chemical (Fig 1B) Dichloracetic acid is a liquid which is used full strength. Trichloracetic acid is used as a saturated solution.

The amount of keratolytic required to penetrate the keratin layer depends on the thickness of the cornified layer If it is thick, as on the palmar and plantar surfaces, or if there are horny scales or projections repeated application of the acid and scraping with a dull knife may be required. The penetration of the keratin layer is signalled by the whitening of the skin, an effect produced by the coagulation of the protein in the cells of the prickle cell layer

Some heavily keratinized squamous cell carcinomas have thick, impenetrable deposits of keratin which must be removed to allow penetration of the acid. Ulcerated surfaces ordinarily do not need treatment with a keratolytic unless the neoplasm is believed to contain considerable amounts of keratin.

Application of the Fixative Chemical

For fixation of the tissues in situ, zinc chloride fixative paste is applied in a layer the thickness of which depends upon the depth of penetration desired. If the main mass of the cancer has not been removed previously the thickness of the applied layer may be 2 or 3 mm or more, a dose which often is sufficient to penetrate the entire grossly detectable mass within a twenty four hour interval (Fig 1C) If the main mass has been excised previously the thickness of the applied layer may be 1 mm. or less. This dose is sufficient to penetrate ap-

* Obtainable from chemical supply houses such as Eastman Kodak Company Rochester N Y., Fischer Scientific Company Pittsburgh, Pa. and Kay Fries Chemicals Inc. New York, N Y

it is more convenient for the patient to return in twenty-four hours. Familiarity with the rate of penetration to be expected from various doses of the fixative acting over various periods of time allows considerable latitude in the arrangement of treatment schedules.

The penetration of the fixative also is affected by the type of tissue through which it is to penetrate. As previously stated keratin strongly retards the penetration of zinc chloride. For this reason the fixative does not appreciably affect the normal unbroken skin unless the keratin is very thin as, for example, on the eyelids. Fortunately, keratolytics such as dichloracetic acid readily overcome this barrier The keratin in heavily keratinized squamous cell carcinoma retards penetration to a significant extent Similarly, the melanin in densely pigmented melanomas inhibits penetration, but to a somewhat more limited extent. Bone forms a partial barrier to zinc chloride so that the penetration may be less than half as great as that in the adjacent soft tissues. The superficial compact bone is *more resistant to the fixative than the more* porous cancellous bone. Cartilage is very readily penetrated by zinc chloride therefore it is necessary to apply the fixative sparingly when working on the cartilaginous structures of the nose or ear in order to avoid excessive destruction or unnecessary perforation. Muscle tissue slightly retards the penetration of zinc chloride, and this retardation is greater in a direction perpendicular to the muscle bundle than it is along the long axis.

The greater the vascularity of the tissue the less the penetration because the fixative is more rapidly carried away from the area under treatment. Thus, less fixation is expected in inflamed tissues, in highly vascular neoplasms, and in tissues adjacent to large blood vessels. The reduced penetration in the immediate vicinity of blood vessels accounts for the fact that bleeders not infrequently are encountered during the excision of layers of fixed tissue even though the incision is made at a level at which fixation otherwise is adequate.

The converse situation also is true namely that decreased circulation allows greater penetration because less of the fixative is carried away from the area under treatment. For example, the avascular scar tissue produced by radiation with roentgen or radium rays is penetrated much more rapidly and deeply than usual. That this effect is in part caused by the profound endarteritis produced by radiation is suggested by the fact that scars produced by trauma, burns or operations are not penetrated as rapidly although they too are somewhat more rapidly penetrated than normal tissue. The peripheral circulatory impairment which leads to gangrene in arteriosclerosis, diabetes, etc. also renders the tissues more penetrable by the fixative Some tissues such as fat and cartilage are naturally less vascular than others and this, in part at least, accounts for the more rapid penetration through these structures. The action of the fixative on vessels which supply isolated structures such as the nasal ala or the helix of the ear may produce localized ischemia with the result that penetration may be excessive in these structures if this effect is not taken into account and correspondingly smaller doses used The vasoconstriction produced by the *adrenalin sometimes used in procaine* solutions may cause accelerated penetration for an hour or more. For this reason, and also because it may cause delayed separation of the final layer of fixed tissue, adrenalin ordinarily is not used. Obviously when it is realized that a less vascular tissue may be encountered, it is necessary to reduce the amount of fixative or reduce the length of time it is allowed to act.

Tissues which readily become edematous when acted upon by the fixative are penetrated less because of the dilution of the chemical by the tissue fluid. In effect, the swelling of the tissues increases the distance the fixative has to penetrate. This effect sometimes is *useful* as, for example, in the treatment of lesions on the eyelids where the lid edema and the chemosis push the treated area away from the eyeball and thus provide an extra margin of safety Firmly knit tissues as for example those of the fingers and those of scars, cannot swell and hence are more readily penetrated by the fixative which accordingly must be more sparingly applied.

Wetness of a treated surface, obviously tends to dilute or wash away the fixative chemical. Lesions of the mouth, nasal cavity eyelids,

larynx and vulva present technical problems because of this dilution effect. Some salivary gland tumors produce so much saliva that the fixative must be applied at more frequent intervals to overcome the dilution effect of the secretion. In infected lesions there may be sufficient exudate to dilute the fixative and reduce penetration.

The atmospheric humidity has an effect on the penetration of the fixative if the occlusive dressing is not kept in place. The effect varies with the level of the relative humidity. Since zinc chloride is highly deliquescent, the fixative becomes excessively liquified upon exposure to the humid atmosphere of the summer months. The dry atmosphere produced by artificial heating in the winter tends to cause the paste and the fixed tissue to dry to a hard mass. Lesions around the nares are especially prone to drying because of the constant passage of air over the surface. Both excessive liquefaction and excessive drying can cause a reduction of the penetration of the fixative. To avoid the effects of variations in humidity the dressings must be occlusive and must be applied in such a way that they remain in place for the period of action. If the dressing is lost inadvertently, the drying effect of the air may be obviated by spreading petrolatum on the lesion.

The list of factors affecting penetration may seem formidable but with daily use of the method it soon becomes second nature to integrate them into a determination of the correct dosage for the individual lesion.

Application of the Occlusive Dressing

The area to which the fixative has been applied is covered with a thin layer of cotton to hold the paste in place. This, in turn, is covered with an overlapping dressing consisting of cotton with petrolatum spread on the under surface to make an airtight closure. It is convenient to have the cotton backed with gauze for the outer covering. The dressing is securely fastened with waterproof adhesive tape. As the tape is applied care is exercised to follow the anatomic contours and to allow for changes in shape if the area is subject to motion (Fig 1D). In general the dressings should be no larger than necessary and they should be accurately and securely placed (Fig 2).

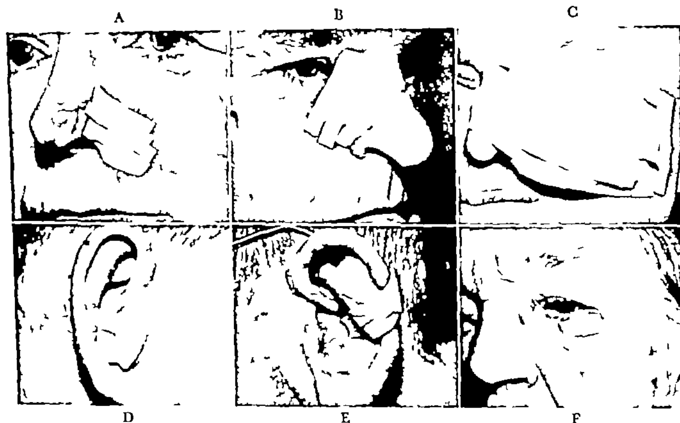


Fig 2 Examples of occlusive dressings used to hold the fixative in place.

Analgesia During the Period of Fixative Penetration

Often no analgesia is required during the period in which the fixative is penetrating through the tissues, but if the lesion is large or in a sensitive area an analgesic should be available to the patient. *Aspirin may suffice for mild* discomfort, but more often a combination of aspirin 10 grains (0.6 gm.) and codeine phosphate, ½ or 1 gr (30 or 60 mg) is prescribed for use at intervals of two or three hours as needed Equivalent preparations such as codempiral may be prescribed but proprietary preparations containing caffeine should be avoided because they may cause insomnia. Very advanced lesions may necessitate hospitalization of the patient so that adequate doses of morphine or morphine like drugs can be administered.

Excision of the First Layer of Fixed Tissue

After the fixative has been allowed to penetrate for a suitable period of time the first layer of fixed tissue is excised with a scalpel. There is no pain or bleeding because the incision is made through killed and fixed tissue and not through the underlying viable tissue. If the incision inadvertently is carried too deeply bleeders may be encountered but these are rapidly controlled by the application under momentary pressure of small squares of gauze impregnated with zinc chloride fixative. Bleeding from larger vessels such as the superficial temporal, labial or external maxillary arteries requires the somewhat longer application of pressure, while bleeding from still larger vessels may require suture-ligatures.

If there is sufficient cancer present after the first excision to be recognized grossly by its whitish color and its friable consistency (Fig 1E) the fixative is reapplied immediately since no systematic microscopic study of the area is required However vertically cut frozen and paraffin sections are made routinely for histopathologic studies (Fig 1F) The depth of the reapplication of the fixative depends upon the amount of cancer which is thought to remain. If a large amount obviously is present, a thick layer is applied but if only a small amount is expected the fixative is applied in a thickness just sufficient to allow the removal of specimens 1 to 2 mm. thick for microscopic study

Excision of the Second Layer of Fixed Tissue

If during the excision of the second layer of fixed tissue it is observed that no grossly visible cancer is present (Fig 1G) the next step is the systematic microscopic examination of the entire area. This important part of the treatment is accomplished by excising a layer of tissue for frozen sections. During the removal of this layer the tissue is divided into specimens about 1 cm. square, a size which is convenient for the technician to section and for the operator to examine.

Mapping the Lesion

The origin of each specimen of fixed tissue is indicated on the lesion by means of mercurochrome (merbromin) which shows up well against the grayish white background formed by the fixed tissue (Figs. 1G 1H and 1J) The origin of the specimens also is indicated on a map which is drawn on a pad of paper by the operator or by an assistant. The specimens are assigned consecutive numbers on the map, and this order is maintained as the sections are made. In order to designate right from left and superior from inferior dyes are applied to the edges of the specimens. These coloring materials adhere through the sectioning procedures and may be seen on the sections upon both gross and microscopic examination. The locations of the colored edges are indicated on the map by means of symbols as follows solid lines for red dye (mercurochrome) dotted lines for blue dye (ordinary washing bluing which is soluble Prussian blue or ferrous ferrocyanide) and wavy lines for black (India ink) Usually orientation *is adequate when one or two edges* are marked but not infrequently three edges are colored. Often epithelium, cartilage or some other distinguishing tissue structure serves to indicate one edge of the specimen.

The shape of the specimens may vary considerably but it is advisable to avoid very irregular shapes because of the danger of losing

some part of the specimen during the sectioning process. The size of the specimens depends on the nature of the tissues. If the tissue is soft and friable smaller specimens are taken to reduce the chance of losing a portion of the specimen. If the tissue is firm, the specimens may be as large as 2 cm. square. The importance of complete sections cannot be too strongly stressed because the loss of even a small cancer-containing portion of a specimen might be the cause of recurrence.

Examination of the Frozen Sections

After the specimens have been removed and the map of the lesion drawn the surface of the wound is covered with moist cotton to prevent excessive drying The patient then waits until the frozen sections have been prepared by the technician and examined by the operator

As will be more fully described in a later chapter on microtechnic, the specimens are placed upside down on the microtome stage so that the *under* surface of the flat specimen is cut. If microscopic examination of these sections reveals cancer at any point, it is presumed that the corresponding point in the immediately subjacent tissue on the patient also contains cancer

The scanning of the sections must be carried out systematically so that no area is missed Some operators prefer to accomplish this by the use of a mechanical stage on the microscope, but with experience it is possible to scan the sections a little more rapidly and just as accurately without this device The usual procedure is to begin with a sweep along one edge and then go back and forth in lines parallel to this edge until the entire specimen has been examined The low power objective ordinarily is used, and if the section is intact, it takes but a few moments for a thorough examination If the specimens have been friable a part of some of the sections may be missing. In this case it is customary for the technician to place several pieces of tissue on the slide so that the operator may piece together a complete picture of the section.

As areas of cancer are found their location is marked in red pencil on the map (Fig 1H)

Reapplication of the Fixative to the Areas of Cancer

The fixative is reapplied only to the areas in which cancer has been demonstrated microscopically (Fig 1H) This limitation of treatment to the cancerous areas is an important feature of the method because by virtue of it, essentially selective destruction of the neoplasm is possible

The individual areas to which the fixative has been applied then are covered with cotton and the entire lesion again is covered with a petrolatum-spread gauze backed cotton dressing

Excision and Microscopic Study of Subsequent Layers

After an interval which may vary from a few minutes to forty-eight hours, a layer of fixed tissue is excised from the treated areas (Fig 1J) If the frozen sections indicate that these areas still contain cancer another application of the fixative may be required. Sometimes, many more applications and excisions are necessary before the entire area becomes free of cancer As will be pointed out repeatedly external neoplasms often send out slender outgrowths into the interstices of the surrounding tissues and, since these often are not clinically detectable their sure eradication can be accomplished only by the microscopically guided excisions which characterize the chemosurgical method

Cancer tissue ordinarily is readily recognized under the microscope, but it is possible for an inexperienced operator to confuse the terminal extensions of a cancer with such non-neoplastic structures as sweat glands sebaceous glands, salivary glands, collections of leukocytes, hair follicles and obliquely-cut epidermis (Fig 3) With experience gained from the constant use of the method however such difficulty is rarely encountered.

If the cancer extends deeply instruments other than the ordinary scalpel and forceps may be required. For deep excavations the scalpels, forceps and scissors should have long slender handles. Usually the flat layers of tissue can be excised from deep lesions with straight knives

but occasionally blades with a bend approximately one centimeter from the tip are helpful Detachable blades may be bent by holding the tip with a pliers while heating the adjacent metal with a fine gas flame For the removal of bone, rongeurs are used if an adequate grasp can be secured otherwise, a chisel and mallet are employed.

The invasion of bone by the neoplasm usually is manifested by pitting and honeycombing which is grossly visible. If there is doubt, however a layer of bone may be removed with a chisel and frozen sections made using an old microtome knife which is kept for this purpose. Decalcification before sectioning ordinarily is too slow to be practical. Often it is possible to

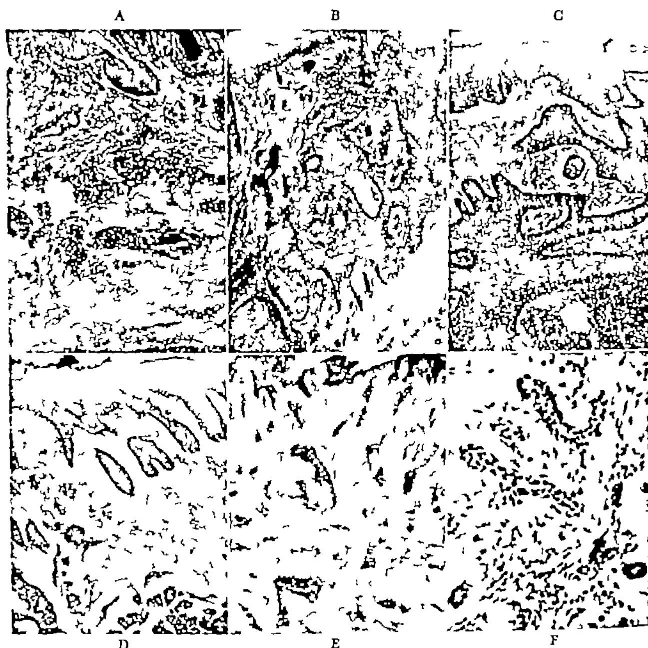


Fig 3 Frozen sections which exhibit non-neoplastic structures that may be mistaken for cancer by the inexperienced operator (A) Collections of lymphocytes and plasma cells which simulate basal cell carcinoma. (B and C) Obliquely-cut rete ridges, hair follicles and sebaceous glands which simulate squamous cell carcinoma (D) Obliquely-cut rete ridges (upper right) which are to be distinguished from the basal cell carcinoma (lower and left) (E) Small vessels with perivascular infiltrate and (F) nasal mucosal glands which are to be distinguished from basal cell carcinoma.

make frozen sections of small bits of soft tissue removed from eroded portions of the bone to determine whether the erosion is being produced by cancer or by some other process.

If a large vessel has been entered or closely approached during chemosurgical treatment, it is advisable to place a suture-ligature around it to avoid hemorrhage when the final layer of fixed tissue begins to separate. Visual or palpable pulsation usually indicates the point at which the suture is needed. Occasionally, the ligation of an artery proximal to the lesion is indicated.

When a cancer free level is reached (Fig 1J) there remains a thin layer of fixed tissue which usually is kept covered with double thickness petrolatum gauze to obviate the drying effect of the air. Often the dressing is left in place until the patient returns several days later for removal of the final layer of fixed tissue. Sometimes the patient, a relative or the family physician is instructed to replace the dressings as necessary. He is told to clean the skin around the wound with a cleaning fluid, such as carbon tetrachloride or benzine, to remove the oil of the skin so the adhesive tape will stick. The petrolatum is spread on a layer of gauze and this is placed against the lesion. If the wound presents an excavation, the depression is filled in with cotton. Finally gauze is placed on the surface and the whole is taped in place. Clean but not necessarily sterile technic is used. The tissues are quite resistant to infection.

If the lesion is small or if it is located in an area where a dressing is difficult to keep on such as on the lip, the lesion may be left uncovered. A small amount of petrolatum may be applied to prevent excessive drying and shrinkage of the final layer of fixed tissue.

Removal of the Final Layer of Fixed Tissue

Several days after the completion of active chemosurgical treatment the final layer of fixed tissue becomes loose so that it may be removed by clipping the remaining adherent strands with sharp-pointed scissors (Fig 1K). A fixation forceps with a serrated grasping tip is useful for holding the tissue being removed. Usually this procedure may be carried out without the necessity of a local anesthetic. At times, however a sensitive nerve may have to be cut to free the layer of tissue and in such cases the injection of a small amount of procaine is desirable. Sometimes the application of a pledget of cotton soaked in 10 per cent cocaine to the sensitive area provides sufficient anesthesia.

If large vessels have been encountered in the course of treatment these may be opened during the removal of the final layer of fixed tissue. If the bleeding is moderate, oxycel cotton may provide adequate hemostasis, but if the bleeding is active a suture ligature may be necessary.

If the lesion is not large and no complications are expected, the final layer of fixed tissue may be allowed to separate spontaneously. This is commonly done if the patient lives a long distance from the clinic. If there is a possibility of active bleeding or if there are structures such as cartilage or bone which must be removed, the patient is requested to return to the chemosurgeon or to report to his family physician to whom is sent a note containing instructions regarding the care of the lesion. If there is any possibility of hemorrhage from small vessels, a supply of oxycel cotton may be provided and the patient instructed as to its application under pressure over the bleeding point.

Factors Affecting the Time of Separation

The final layer of fixed tissue separates more rapidly in tissues with a loose connective tissue stroma than in those with a dense fibrous framework. Thus fixed tissue separates rapidly from the lip (average 4.4 days) and from the eyelids (average five days) while from the back, separation is very slow (over ten days). Intermediate rates of separation are exhibited by other areas such as the extremities (average six days), the face and head (average 6.3 days) and the ears (average seven days).

If the main mass of cancer has been surgically removed and a relatively short period of chemosurgical treatment has supervened, separation requires one to three days longer. If adrenalin has been added to the procaine solution used for local anesthesia, the rate of separation is retarded still further. Somehow the chemical inflammation produced by the prolonged use of the fixative serves to

shorten the time required for separation, perhaps by stimulation of the formation of the autolytic enzymes concerned with dissolution of the tissues at the line of separation.

Fixed cartilage and bone are not thrown off as rapidly as the fixed soft tissues. Usually cartilage must be removed at the appropriate level by means of a scalpel or scissors in order that granulation tissue may grow across and epithelization proceed unhindered. A line of demarcation forms between fixed and unfixed bone in two to three weeks. When this occurs the layer of fixed bone may be grasped with a forceps or a rongeur and by means of a rocking motion lifted off as an intact sheet. By the time separation occurs, the underlying bone is covered with healthy granulation tissue.

Tendons, ligaments and other densely fibrous structures are not rapidly thrown off by the tissues of the body and therefore, they must be excised so that rapid healing may take place. However if it is desired to preserve the function of a tendon or ligament, the structure may be left intact and even though it has been killed and fixed by the zinc chloride, it will remain functional after it has been bridged over by the granulation tissue and skin.

Tissues which have received large doses of roentgen or radium rays are appreciably slower to separate than the corresponding normal tissues. This slowing of separation is most striking in the case of bone which may require two or three months instead of the usual two or three weeks to separate. Sometimes irradiated bone is so slow to loosen that it is necessary to forcibly remove as much as possible with a rongeur or chisel so that islands of granulation tissue may form. Intervening fragments of fixed bone may be removed later or they may be allowed to cover over with granulation tissue and epithelium. In the latter case spicules of bone may push through to the surface after the elapse of months or years.

Fortunately the tissues adjacent to those killed by zinc chloride are not damaged hence, the fixed tissues are thrown off relatively rapidly By contrast, tissue killed by heat requires twice as long to separate, while tissue killed by roentgen or radium rays requires many times as long to demarcate from the adjacent viable tissues. Apparently, the reactivity of the tissues beyond the level of actual necrosis is impaired by the action of heat or irradiation.

After-care of the Wound

The granulation tissue exposed as the final layer of fixed tissue separates is remarkably vascular and is highly resistant to infection. The lesion at this stage ordinarily is dressed with scarlet red ointment impregnated gauze. This dressing material is a modification of that described by Bettman.[14] The ointment which is used to impregnate the gauze consists of the following

Oxyquinoline sulfate	25
Chlorbutanol (chloretone)	100
Scarlet red	250
Anhydrous woolfat	1500
Petrolatum	3000

The oxyquinoline sulfate is dissolved in 200 cc. of hot water and added to the melted woolfat. This in turn is added to the melted petrolatum. The chlorbutanol is dissolved in 100 cc. alcohol and added to the mixture. Because of the heat the alcohol evaporates. The scarlet red powder is wetted with some of the mixture to allay the dust and then is stirred in and mixed in a mixer until the ointment is nearly solid. The sterilized strips of two-inch fine-mesh gauze are cut into six inch lengths and impregnated by placing them in a 3 × 8 inch pan and covering them with the ointment. The pan of strips is warmed just enough to cause even permeation through the gauze.

This dressing material has proved quite satisfactory during the fifteen years it has been in use in the Chemosurgery Clinic. It provides mild antiseptic and anesthetic effect in addition to a slight but definite stimulation of epithelization. The contained ointment prevents sticking to the granulation tissue except in the occasional case in which the granulations are excessively wet. In the latter event there may be a tendency for some of the fibers of the gauze to be incorporated in the granulation tissue unless they are removed. Occasionally under similar circumstances, particles of scarlet red may become enmeshed in the granulation tissue producing a tatoo which may require several months to absorb. Another complication which

is observed once in every four or five hundred cases is a drug hypersensitivity which is manifested by a weeping dermatitis in the immediate vicinity of the lesion. This reaction subsides promptly with the use of boric acid compresses As a rule sensitivity reactions occur in cases in which an excessive amount of the gauze has been used over a prolonged period of time For this reason the gauze should be cut to the exact size of the area of the granulation tissue only one thickness of the gauze should be applied and it should be discontinued as soon as healing is complete.

The dressing which is applied over the single layer of scarlet red gauze, consists of gauze or of gauze backed cotton. Mild pressure on the healing surface is beneficial. If there is a depression it is lined with scarlet red gauze and then packed with sterile cotton to provide even pressure over the granulating surface. Scarlet red gauze should not be applied to areas in which fixed tissue still is adherent because it inhibits the enzymes which effect separation of this tissue.

No dressings are necessary for small lesions. It is sufficient to apply an aqueous solution of mercurochrome to provide a protective, antiseptic crust. A dry gauze dressing may be applied if desired for cosmetic purposes or for protection of the clothes. Prepared dressings such as Bandaids often are useful for this purpose.

Occasionally the granulation tissue becomes elevated above the level of the skin. If not removed this exuberant tissue can delay healing and lead to excessive scar formation. Cauterization with a silver nitrate stick ordinarily is sufficient.

Defects produced during chemosurgical treatment quickly fill in and epithelization is surprisingly rapid. Because of this prompt healing the resulting scars are soft, pliable and much less noticeable than one would expect (Fig 1L) On the skin the scar remains pink for several weeks and then gradually fades out to approximately the color of the surrounding skin. On mucosal surfaces the scar is covered with mucosa which often makes it invisible except upon blanching by pressure.

From the considerable amount of detail given here concerning the chemosurgical technic it may be thought that the method is unduly involved and time-consuming Actually, the treatment is completely practical and in a well organized clinic it can be carried out in far less time than it takes to tell about it. Although a certain amount of meticulous attention to detail is an unavoidable disadvantage, the increased reliability, the conservatism and the low risk are compensatory advantages. Some of the details of treatment have only been mentioned but they will be elaborated in the text and in the descriptions of the figures in subsequent chapters.

Plastic Repair of Defects Following Chemosurgical Treatment

Occasionally circumstances warrant an immediate plastic repair For example a defect through the lower lip might cause downward retraction of the lip and difficulty in eating unless the defect were immediately repaired with a flap (Fig 31) Or a large lesion of the forehead and scalp might require too long to heal and might cause upward retraction of the eyebrow This could be avoided by the application of a split thickness graft (Fig 12) Often the certainty of removal made possible by the microscopically controlled chemosurgical excision of the cancer justifies earlier repair than otherwise would be considered safe. However, if the cancer has recurred in scattered sites after previous surgical or radiation treatment and if there is considerable likelihood of other outlying disconnected neoplastic foci being present, it is advisable to delay the repair until it is felt certain that there will be no more outcroppings. Fortunately if there is to be a recurrence after chemosurgical treatment it becomes manifest quite promptly It is not buried deeply under an incisional scar as may be the case following surgical excision nor is it entrapped in a dense, atrophic scar as may be the case following radiation therapy Accordingly a period of delay of six to twelve months usually is sufficient.

Surgical Excision with Microscopic Control

For certain small lesions in sites where the wound may be closed readily with sutures it may be expedient occasionally to assure com

plete removal by the use of frozen sections through the under surface of the excised specimens. A map is drawn on a pad of paper to show the origin of the specimens the same as in the chemosurgical technic. The wound may be left open, perhaps with the sutures inserted but not tied until the sections have been examined. Then if cancer is revealed another layer may be excised from the involved area, and the procedure repeated until a completely cancer free level has been reached. This technic is suitable for small nodular basal cell carcinomas where there is relatively little chance of spreading the neoplastic cells through the incision. However it is not recommended for anaplastic basal cell carcinoma or for squamous cell carcinoma and it is absolutely contraindicated for lesions in which melanoma is suspected. Since the fresh tissues are much more difficult to handle and to section than tissues which have been fixed in situ, the procedure is limited to small discrete lesions. At this point it may be mentioned that the use of representative sections of the periphery of excised specimens is not a new practice,[78,80] but such incomplete appraisal of the peripheral tissues cannot approach the degree of reliability that may be attained with complete sections.

Care of the Regional Lymph Nodes

With squamous cell carcinoma melanoma and sarcoma the possibility of metastasis must always be kept in mind.

Enlargement of regional nodes may signify metastasis but it also may be produced by lymphadenitis. If the nodes consist of definite hard masses, the diagnosis of metastasis may be quite obvious and dissection of the node-bearing tissues clearly is indicated. However if the nodes are small and not very hard and if the primary lesion is small and not very highly malignant, there may be considerable doubt as to whether the nodes are cancerous or simply inflamed. In such a case it may be justifiable to delay the node dissection and observe the patient for a few weeks. Of course the patient must not be lost track of and if he does not return as directed he must be traced and persuaded to return. If the enlargement persists unchanged or increases after the primary lesion has healed, a regional node dissection is in order

Prophylactic dissection of regional nodes occasionally is indicated if the size and degree of malignancy of the primary lesion are sufficient to suggest a strong possibility of metastasis. The microscopic appearance of the primary neoplasm may give some indication of the possibility of metastasis by such details as the degree of anaplasia the size of the cells, and the thickness and integrity of the walls of the blood vessels and lymphatics. Other factors such as the amount of motion of the primary site and the type of the neoplasm also affect the degree of likelihood of metastasis. A more complete consideration of the various factors which play a part in reaching a decision regarding prophylactic dissections is discussed in subsequent chapters.

Dissection of regional nodes ordinarily is a surgical procedure but occasionally nodes are so situated that chemosurgical excision is indicated. Examples which may be cited are (1) a case of submaxillary node metastasis of squamous cell carcinoma with firm fixation to the mandible (Fig 120) and (2) a case of preauricular node metastasis of melanoma with invasion in the vicinity of the temporomandibular joint (Fig. 152) Sometimes the nodes in one region may be removed chemosurgically and those in another region may be removed surgically Thus, in the second case just cited, the patient was referred for surgical dissection of the cervical nodes because these could not be removed chemosurgically on account of the proximity to the carotid and jugular vessels.

Observation of Patients after Treatment

It is routine in the Chemosurgery Clinic to follow all patients who have had cancer for at least five years. This practice serves two main purposes first, any recurrent or metastatic focus is promptly recognized and treated and, second, significant statistical data as to the efficacy of treatment is accumulated. In addition, this practice often permits early recognition of other newly-developed primary lesions.

No fixed routine for check-up visits is followed Rather the observation schedule is individualized for each patient. If the patient

has had a small or medium sized, uncomplicated basal cell carcinoma he usually is asked to return in six months. However, if the patient has had a squamous cell carcinoma he usually is asked to return in three months. Patients with large complicated lesions might be asked to return in one month or even less. In addition, the patients are acquainted with the manifestations of recurrence or metastasis, and they are instructed to return at once if such symptoms arise. As time passes without evidence of recurrence or metastasis, the intervals between check up visits are increased to six or more months. If the patient must come from a long distance his progress is followed by correspondence with him or his family physician. Sometimes, considerable detective work is necessary to trace migratory patients and to determine the cause of death of deceased patients.

The determination of the rate of cure after five years is made from the results obtained in the "determinate" group of cases. This group includes the unsuccessful results (patients dead as a result of cancer patients with cancer lost from observation, and patients living with cancer) and the successful results (patients free of cancer for five years or more) Not included in the determination of the cure rates are the "indeterminate" group of cases which includes the patients who died of other causes without recurrence of the cancer and the patients who were lost from observation without recurrence. These indeterminate cases are excluded from the calculations of the rate of cure because there is no way of ascertaining what the outcome would have been if the period of observation had been five years. However, if the patients of this group had not died or had not been lost it is likely that the rate of cure would have been at least as high as that calculated for the determinate group

General Indications for Chemosurgery

The chemosurgical technic is indicated for most cancers on the external surface of the body It also is indicated for many cancers in cavities accessible through normal artificial or pathologic openings if technics can be devised to hold the fixative preparation in place. Thus most carcinomas, melanomas and sarcomas of the skin are amenable as are neoplasms of the lips, oral cavity salivary glands, nasal cavities accessory sinuses, larynx, vulva, vagina, penis and anus. Cancer of the breast, though an external lesion is not amenable to chemosurgical treatment because of the mode of lymphatic spread which necessitates radical mastectomy an operation best carried out with the usual surgical technics. Local recurrences following mastectomy however often may be treated advantageously by means of the chemosurgical method. This list of indications is not necessarily exhaustive and other uses for the technic are being found constantly

Cancers affecting various regions of the body exhibit individual characteristics and responses to treatment. Accordingly the chemosurgical treatment as it relates to each area is discussed in the chapters which follow

CHAPTER 3

Carcinoma of the Face, Scalp and Neck

CANCERS of the face, scalp and neck[44] are considered as a separate group because they are located on regularly contoured readily accessible surfaces where treatment is less complicated than on the irregular circumorificial surfaces presented by the nose ears, eyelids and lips which are discussed in later chapters. Reflecting the relative paucity of complications met during the treatment of carcinoma of the face scalp and neck are the excellent therapeutic results as indicated by the statistics given at the end of this chapter

Forehead, Temple and Scalp

The relatively thin layer of soft tissues stretched over the unyielding cranium in the regions of the forehead temple and scalp sets these areas apart from other regions of the face. Perhaps partly as a result of this disposition of the tissues, the cancers in these regions often have a tendency to spread more extensively in a peripheral rather than in a deep direction. This type of spread is most common among the more highly invasive basal cell car

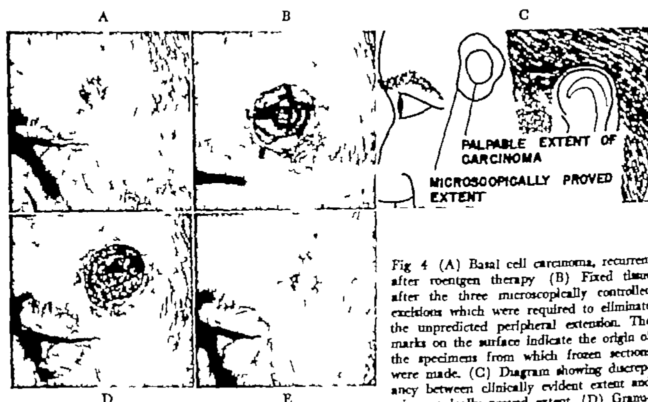


Fig 4 (A) Basal cell carcinoma, recurrent after roentgen therapy (B) Fixed tissue after the three microscopically controlled excisions which were required to eliminate the unpredicted peripheral extension. The marks on the surface indicate the origin of the specimens from which frozen sections were made. (C) Diagram showing discrepancy between clinically evident extent and microscopically proved extent. (D) Granulation tissue after separation of the final layer of fixed tissue. (E) Healed lesion. There was no recurrence after 2 years.

cinomas which often exhibit a distinct affinity for the dermis and upper subcutaneous tissue

The tendency of basal cell carcinoma to spread in a peripheral direction is nowhere greater than on the forehead and on the ad from one lesion to another, and it even varies in different sectors of the periphery of the same lesion (Figs. 5 and 6) Previous irradiation often accentuates the tendency for silent peripheral spread because it may allow superficial healing

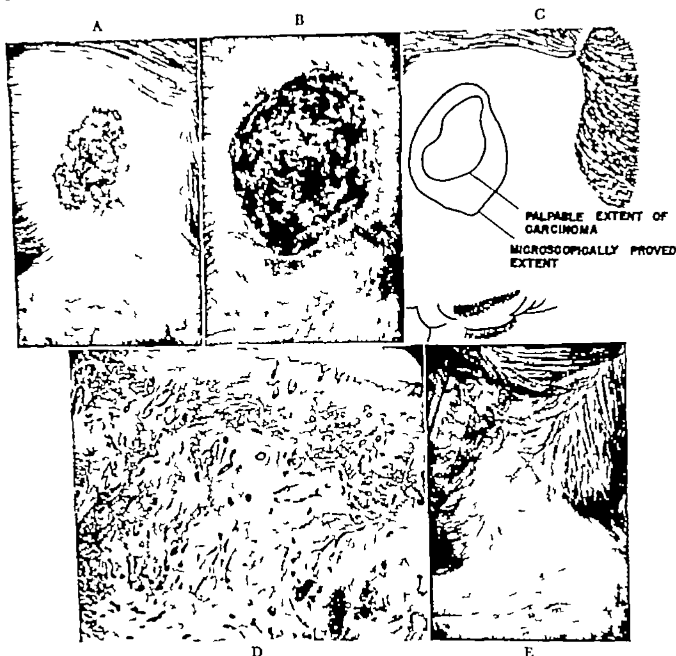


Fig 5 (A) Basal cell carcinoma, apparent size 31 × 51 mm. (B) Granulation tissue after separation of final layer of fixed tissue The five chemosurgical excisions revealed peripheral extension to an area which measured 54 × 75 mm. (C) Diagram showing discrepancy between palpable extent and actual extent. Note variation in the width of the "silent" zone at different portions of the periphery (D) Photomicrograph showing invasive strands in dermis. (E) Healed lesion. There was no recurrence after five years.

jacent scalp and temples. This peculiarity may be exhibited by relatively small lesions (Fig 4) but it is more striking as the lesions become larger (Fig 5) The amount of "silent" extension into the dermis varies considerably while the cancer continues to spread in the deep dermis and subjacent subcutaneous connective tissue (Fig 6) With the peripheral spread being so unpredictable the microscopic control afforded by the chemosurgical technic is

invaluable. In many cases the central part of the lesion may become cancer free with the initial excision while some portions of the periphery may not become free of cancer until many more layers have been excised.

Some carcinomas in this region invade to the superficial fascia and then spread peripherally in the lumens of the lymphatic vessels tend for many centimeters along the periosteum forming a thin sheet of cancer which cannot be differentiated from the underlying cranium either by gross visualization or by palpation. In such cases the overlying skin also must be sacrificed except insofar as the periosteum can be removed by undercutting

Although the tendency to spread peripherally

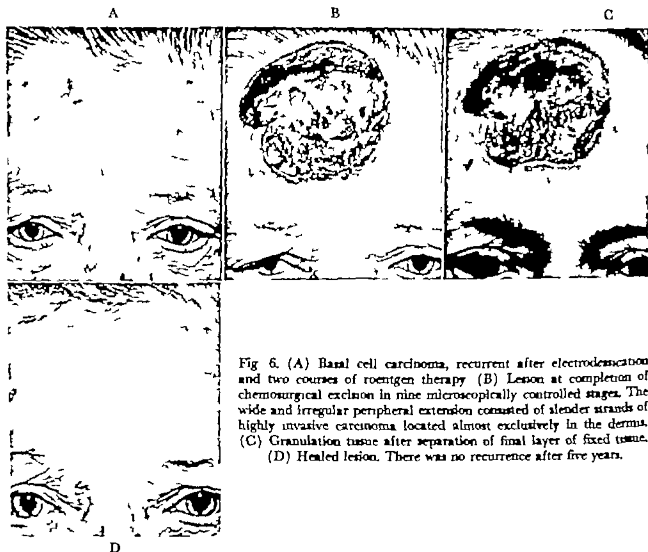


Fig 6. (A) Basal cell carcinoma, recurrent after electrodesiccation and two courses of roentgen therapy (B) Lesion at completion of chemosurgical excision in nine microscopically controlled stages. The wide and irregular peripheral extension consisted of slender strands of highly invasive carcinoma located almost exclusively in the dermis. (C) Granulation tissue after separation of final layer of fixed tissue. (D) Healed lesion. There was no recurrence after five years.

which form a plexus at this level (Fig 7) To get at this layer some of the overlying skin and subcutaneous tissue must be removed but as the termination of the outgrowths are approached a certain amount of undercutting may be done to preserve as much of the overlying skin as possible.

Other carcinomas invade to the periosteum and then extend peripherally along this structure. In some cases the neoplasm may ex-

is more characteristic of the highly invasive, basal cell carcinoma it also may be exhibited by squamous cell carcinoma (Fig 8) While the latter type of carcinoma usually does not have any particularly selective affinity for dermis, lymphatic plexuses or periosteum, its spread may be predominantly centrifugal because barriers to vertical extension are imposed by the galea aponeurotica, the periosteum and the cranium. These barriers are more effective

against carcinomas with a low degree of malignancy than they are against those with a higher grade of malignancy

Some highly invasive carcinomas may erode through all of the layers covering the cranium in a relatively short time while some less invasive cancers may reach the cranium only after a long period of slow growth (Fig 9) In either event the required exposure of the skull may be accomplished readily and safely by means of the chemosurgical technic.

In the absence of grossly visible pitting or honeycombing of the outer table of the cranium no further application of the fixative is necessary In the process of removing the periosteum, however, a thin layer of bone unavoidably is killed by the fixative In two or three weeks this thin sheet of fixed bone becomes demarcated from the underlying bone so that it may be lifted off by means of forceps, rongeur or chisel.

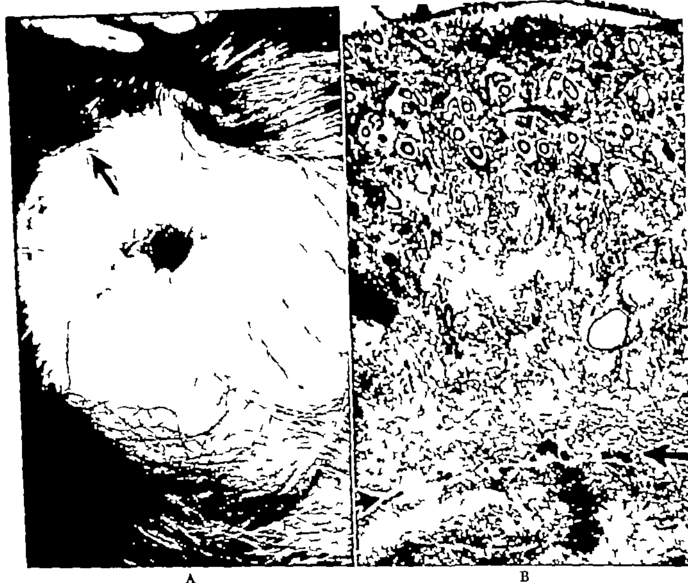


Fig 7 (A) Basal cell carcinoma that had recurred in the central and peripheral portions of a graft The peripheral recurrence (arrow) was not clinically detectable. (B) Photomicograph of frozen section showing invasion in a lymphatic plexus located in the fascia just superficial to the galea at the edge of the graft. There was no recurrence when the patient died of other causes after three years.

If pitting of the bone is grossly visible the abnormal area may be investigated microscopically either by means of sections of the soft tissue dug out of the depressions in the bone or by means of sections of the bone itself In the latter case the specimens usually are removed with a chisel Frozen sections of small



Fig 8 (A) Squamous cell carcinoma, grade 3 (B) Granulation tissues after chemosurgical excision. Despite the wide peripheral involvement the pericranium was not affected. (C) Healed lesion. There was no recurrence after five years.

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Fig 9 (A) Basal cell carcinoma of twenty two years duration. (B) Lesion after chemosurgical excision. The area of invaded pericranium was 2 cm. in diameter (C) Photomicrograph of the relatively noninvasive basal cell carcinoma. (D) Healed lesion. There was no recurrence when the patient died of other causes after three years.

pieces of bone may be cut with an old microtome blade which is reserved for this purpose However frozen sections of large areas of bone are unsatisfactory and if such sections are needed the tissues may be decalcified and paraffin sections made Particular care is required in the microscopic investigation of suture lines and of foramens because these are zones softening of the cerebral tissue. This is particularly the case if the presence of carcinoma makes it necessary to continue chemosurgical treatment peripherally in the dura. Therefore, in such cases the surgical removal of the area en bloc with closure of the defect with a flap may be the preferred procedure provided the surrounding tissues have not been damaged by

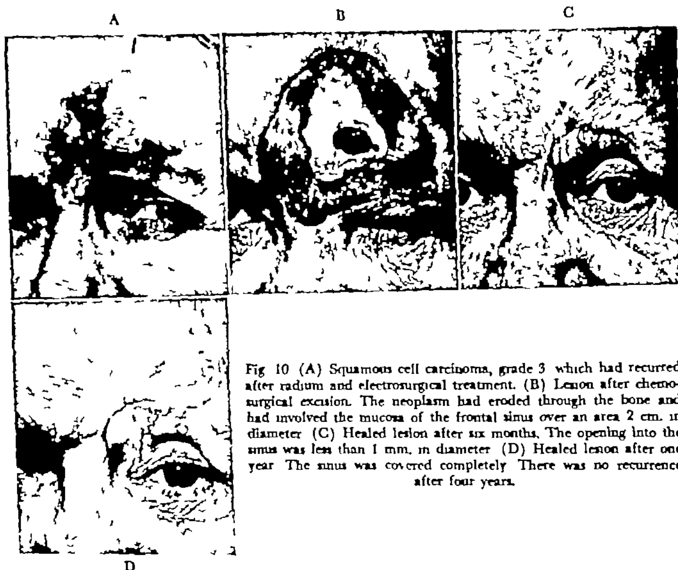


Fig 10 (A) Squamous cell carcinoma, grade 3 which had recurred after radium and electrosurgical treatment. (B) Lesion after chemosurgical excision. The neoplasm had eroded through the bone and had involved the mucosa of the frontal sinus over an area 2 cm. in diameter (C) Healed lesion after six months. The opening into the sinus was less than 1 mm. in diameter (D) Healed lesion after one year The sinus was covered completely There was no recurrence after four years.

of reduced resistance to neoplastic invasion. Bone provides such a good barrier to the invasion of cancer that penetration of the full thickness of the cranium occurs only when the neoplasm has become rather advanced.

Penetration through the cranium with involvement of the meninges and brain is a serious complication but not necessarily a fatal one If the chemosurgically produced opening through the cranium is larger than four centimeters in diameter it is difficult to control the irradiation. Smaller areas of cranium and the underlying membrane and cerebral tissue may be removed chemosurgically with safety if the lesion is located over a non-essential portion of the brain as for example, the frontal lobes. However the removal of portions of the motor area may lead to spastic paralysis and focal epileptic manifestations while a relatively small opening through the cribriform plate of the ethmoid bone may lead to extensive encephalomalacia and death.

Following chemosurgical treatment of lesions with intracranial extensions the final layer of fixed cerebral tissue, along with the fixed meninges, separates in about six days. Shortly thereafter granulations form on the surface of the cerebral tissue and epithelization proceeds rapidly. Strict aseptic precautions are indicated during the period of separation and healing. The resultant soft scar may pulsate noticeably at first, but as the fibrous tissue contracts it pulls the tissues of the scalp tightly over the defect and the pulsation become less evident. Thus far no attempts have been made to cover the cranial defects with metal or plastic plates.



Fig 11 (A) Basal cell carcinoma of twenty-six years duration. It had recurred after several excisions and many roentgen ray treatments. (B) Granulation tissue and exposed cranium after chemosurgical excision in multiple microscopically controlled stages. The neoplasm extended in the dermis far beyond the clinically detectable limits. In the large central area the cancer invaded all of the layers of the scalp and in several areas the bone was slightly eroded. (C) Healed lesion after two years. The skin was unstable and slight trauma caused small ulcers as shown here. Therefore, a flap was shifted from the opposite side of the scalp by Dr W Slaughter. There was no recurrence of the cancer after five years.

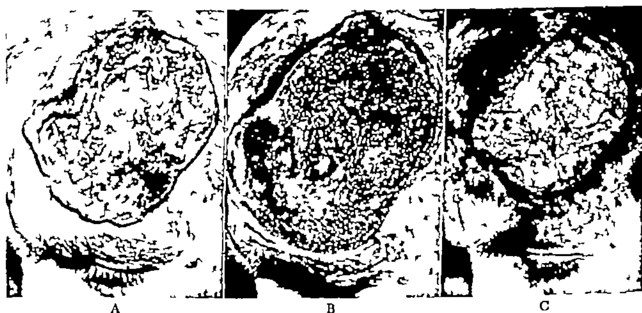


Fig 12. (A) Squamous cell carcinoma, grade 1 in an eighteen year old boy who had sustained fire burns to the forehead and scalp five years before. (B) Granulation tissue at completion of treatment. (C) Split thick ness graft applied without a waiting period by Dr F Bernard. The graft prevented scar contraction and upward retraction of the eyebrow but it did not obscure a recurrent nodule which developed at the medial edge several months later. The nodule was chemosurgically excised and there was no further recurrence after four years.

Neoplasms located over the frontal sinuses may erode through the bone and invade the

sinus mucosa (Fig 10) If most of the lining is involved it may be advisable to remove all of the mucosa so that the wound becomes covered with skin instead of mucosal epithelium. However if the involvement of the head temples and scalp the chemosurgical wounds heal with the formation of scars which are soft, smooth pliable and of good color However lesions over ten centimeters in diameter ordinarily should be covered with split



Fig 13 (A) Basal cell carcinoma which recurred after treatments with caustics and roentgen rays. (B) Granulation tissue after chemosurgical excision. (C) Healed lesion. There was no recurrence after five years.



Fig 14 (A) Squamous cell carcinoma, grade 1 It had arisen in a sebaceous cyst of twenty years duration. (B) Healed lesion. The hairless area is small because of scar contraction. There was no recurrence after 7 years

mucosa is limited only the affected portion is removed. Often the defect will close spontaneously (Fig 10C D) but if not a repair may be required.

Because of the even peripheral tension exerted by the tissues around lesions on the fore thickness or other grafts as soon as possible If this is not done, the contraction of the scar over the unyielding cranium prevents adequate vascularization with the result that the overlying epithelium may be unstable and unduly subject to traumatic ulceration (Fig 11) Large

lesions located just above the eyebrow also should be covered with a graft to prevent undue upward retraction of the eyebrow as scar contraction takes place (cf Figs. 8 and 13) Lesions on the scalp if not too large, should be allowed to heal by second intention because the contraction of the scar considerably reduces the size of the area of baldness (Fig.



Fig 15 (A) Basal cell carcinoma which began on the scalp and extended into the postauricular sulcus. (B) Granulation tissue after chemosurgical excision. The cancer invaded farther than expected into the sulcus and at the superior edge. (C) Healed lesion. The soft smooth scar contracted to a fine linear scar parallel to the sulcus. There was no recurrence after five years.



Fig 16. (A) Basal cell carcinoma which had recurred after radium treatment. (B) Lesion at completion of chemosurgical treatment. Note that the deepest involvement was under the post-radiation scar Also note the wide peripheral extension, especially in the upper half of the lesion. (C) Healed lesion. There was no recurrence after five years.

12) Lesions in the midline of the lower fore head however do not require grafting because they heal with remarkably little tendency to draw the adjacent tissues out of shape (Fig

14) Postauricular lesions of moderate size tend to heal with a fine linear scar parallel to the postauricular sulcus (Fig 15) and even large lesions heal with scars that are unnoticeable.

Because of the underlying temporal fossa, the temple is more subject to deep invasion by carcinoma than are the forehead or scalp. Not infrequently the carcinoma invades to the temporal fascia and then spreads for a considerable distance peripherally in this tissue without invading the underlying temporalis muscle. Occasionally the carcinoma extends downward under the zygomatic arch to the coronoid process of the mandible or to the maxillary bone. In one case a highly invasive basal cell carcinoma followed along the periosteum of the zygomatic arch to the medial *orbital region*. Many of these irregular extensions are not initially detectable and it is only by means of repeated microscopically controlled chemosurgical excisions that they may be located accurately. Even fairly extensive lesions fill in and epithelize rapidly with remarkably good cosmetic results (Fig. 16).



Fig. 17. (A) Basal cell carcinoma with extension into the outer canthal region. (B) Granulation tissue and exposed outer rim of orbit following chemosurgical excision. (C) Healed lesion. There was no recurrence when the patient died of other causes after four years.



Fig. 18. (A) Squamous cell carcinoma, grade 2, which had recurred after treatment *with caustics*. (B) Granulation tissue after chemosurgical excision. There were two clinically undetected outgrowths in the dermis at the upper edge. (C) Healed lesion. There was no recurrence after six years.

Carcinomas which invade the outer canthus may cause some lateral traction on the eyelids but this is of relatively little consequence either from a cosmetic or functional standpoint (Fig 17) Smaller lesions heal with barely visible scars (Fig 18)

In some patients the superficial temporal artery pulsates strongly in the temporal region and if such a vessel is interrupted or closely approached during the course of chemosurgical treatment, there may be sufficient danger of hemorrhage during the separation of the final layer of fixed tissue to make it advisable to place a suture ligature around the vessel Usually the suture is placed by passing it through the fixed tissue into the underlying viable tissue.

Cheek

Carcinomas of the cheek, unless very extensive, are treated easily by means of the outgrowths may be somewhere in the central portion of the lesion or in both the central and peripheral zones (Fig 20)

Extensive lesions may be more difficult to treat because of invasion of adjacent structures but the absence of complicating structures in the cheek makes it feasible chemosurgically to eradicate very advanced lesions (Fig 21) The fact that the microscopic control allows the preservation of a maximum amount of the surrounding normal tissue is especially important for the attainment of a satisfactory cosmetic result Extensive lesions may invade the maxillary sinus and extend in an irregular and unpredictable manner in the mucosa. These extensions are readily followed out by the chemosurgical technic through an opening in the overlying bone. Usually only a part of the mucosa is removed and a fistula may result (Fig 86) If the opening into the sinus is small it may close spontaneously but if it is much



Fig 19 (A) Basal cell carcinoma in a patient with hemophilia. (B) Granulation tissue after chemosurgical excision. There was no bleeding either during excision when the blood was coagulated by the fixative or during removal of the final layer of fixed tissue when the ends of the vessels had healed across. (C) Healed lesion. There was no recurrence after five years.

chemosurgical technic (Fig 19) However though in a site that is readily visualized and palpated, these lesions frequently exhibit silent outgrowths from the main mass. Sometimes the unexpected extension may be predominantly in a peripheral direction, but just as often the over a centimeter in diameter operative closure usually is indicated. Similarly small openings through the cheek may close spontaneously but larger ones require repair (Fig 21)

Smaller lesions in the preauricular region (Fig 22) are not likely to give rise to com-



Fig 20 (A) Basal cell carcinoma of a highly invasive rodent ulcer type. The lesion began on the cheek and extended into the nasolabial fold (B) Granulation tissue after chemosurgical excision. The carcinoma extended deeply into the embryologic fusion plane beneath the nasolabial fold and it extended peripherally in the dermis onto the nasal ala. (C) Healed lesion. There was no recurrence after five years.



Fig 21 (A) Basal cell carcinoma, of a highly invasive sclerosing type. It had recurred after numerous treatments with roentgen rays, radium and electrosurgery (B) Granulation tissue after chemosurgical excision. There were microscopically located extensions involving the parotid gland, the periosteum of the zygomatic bone the anterior edge of the ear and the buccinator muscle. Most of the unpredicted peripheral extensions were into the medial cheek, the lower eyelid and the infra-auricular and mandibular areas. (C) Healed lesion after placement of a graft by Dr W Slaughter The patient was free of cancer after seven years.

plications except in the occasional instance in which considerable pulsation is observed in the superficial temporal artery In that case a suture ligature is placed to prevent hemorrhage during separation of the final layer of fixed tissue.

Deeply invasive lesions in the posterior part of the cheek may necessitate destruction of part or all of the temporomandibular joint (Fig 23) but this is not a serious complication. Destruction of part of the joint capsule or even of some of the joint structures does not



Fig 22 (A) Basal cell carcinoma. (B) Granulation tissue after chemosurgical excision. Unexpectedly deep extension posterior to the ramus of the mandible was demonstrated microscopically (C) Healed lesion. There was no recurrence after nine years.

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Fig. 23 (A) Squamous cell carcinoma, grade 3 *It had recurred after* repeated treatments with roentgen rays and radium. The neoplasm was considered inoperable by several competent surgeons. (B) Lesion during excision of specimen of fixed tissue from over the temporo*mandibular joint. Note the markings made with mercurochrome* on the fixed tissues to show the origin of each specimen. (C) Granulation tissue after separation of final layer of fixed tissue showing exposed zygomatic arch and temporomandibular joint. One outgrowth followed the nerve sheath of a branch of the facial nerve. This branch to the forehead was the only nerve paralyzed during treatment though a considerable amount of parotid tissue had to be removed. (D) Healed lesion. The scar is somewhat thin and atrophic because of the previous irradiation of the area. There was no recurrence after ten years.

appreciably damage the function and there is no danger of ankylosis After the chemically fixed portions of capsule bone and cartilage have been removed granulation tissue grows across the defect and epithelization progresses as usual. The scar is sufficiently soft and pliable to allow good function. If the entire joint must be removed to eliminate the cancer, some malocclusion of the mandible may develop Ordinarily however, this deformity does not seriously impair masticatory function

Advanced lesions of the posterior cheek may necessitate considerable destruction of the ear invaded deeply into the parotid gland These usually close spontaneously within a few days or weeks but if they do not their prompt closure usually can be accomplished by the cauterization of the parotid epithelium with dichloracetic acid and a small amount of zinc chloride fixative. This discourages the parotid epithelium and permits the more vigorous cutaneous epithelium to grow across the defect.

Skin of Upper Lip

Basal cell carcinoma develops much more commonly than squamous cell carcinoma on



Fig 24 (A) Basal cell carcinoma which arose in the skin above the vermilion border and extended downward into the lip proper (B) Healed lesion. There was no recurrence after eight years.

and external auditory canal (Figs. 21 and 23) This ordinarily gives rise to no complications except for the occasional case in which there is some tendency for the canal to become stenotic. Measures to avoid this complication are discussed in the chapter on carcinoma of the ear

If the cancer surrounds any of the branches of the facial nerve their interruption is mandatory However the amount of destruction may be kept at an absolute minimum by the careful employment of the microscopically controlled chemosurgical excisions (Fig 23) Parotid fistulas may result from the chemosurgical removal of carcinomas which have

the skin of the upper lip (the proportion was thirty three to six in this series) The initial basal cell carcinoma usually arises just above the vermilion border and often the neoplasm spreads more rapidly toward the vermilion border than in other directions. This may give rise to the impression that the carcinoma may have originated in the lip proper which is a very rare site for basal cell carcinoma. Careful attention to the history usually enables the distinction to be made (Fig 24) Most basal cell lesions of the upper lip are rather invasive in growing cancers (Fig 25) and this is particularly true of those in the fold between the upper lip and adjacent cheek (Fig 26)



Fig 25 (A) Basal cell carcinoma which had recurred after treatment with caustics and roentgen rays. It was impossible to determine by clinical examination how much of the induration was caused by cancer and how much by scarring from previous treatment. (B) Healed lesion after multiple microscopically controlled chemosurgical excisions which revealed all of the induration to be the result of cancer (C) Lesion after plastic repair by Dr V B. Hyslop showing the favorable cosmetic result made possible by the preservation of maximal amounts of normal tissue. There was no recurrence after five years.



Fig 26. (A) Basal cell carcinoma which had recurred after numerous electrodesiccation treatments and after one course of roentgen therapy (B) Granulation tissue after removal by nine microscopically controlled excisions. The cancer was a highly invasive basal cell carcinoma with several areas exhibiting transition to squamous cell carcinoma. It invaded through the lip to the level of the mucosal glands but did not involve the mucosa. (C) Healed lesion. There was no recurrence after 5 years.



Fig 27 (A) Squamous cell carcinoma grade 2. (B) Granulation tissue after chemosurgical excision. (C) Healed lesion. There was no recurrence when the patient died of other causes after 3 years



Fig. 28 (A) Squamous cell carcinoma, grade 2. It had recurred after two treatments with electrodesiccation. (B) Granulation tissue after chemosurgical excision. The microscopic sections revealed carcinoma in the apparently normal dermis at the superior and medial edges. (C) Healed lesion. There was no recurrence after three years.

Squamous cell carcinoma in common with basal carcinoma often tends to grow downward into the vermilion border (Fig 27)

Chin and Skin of Lower Lip

Cancer of the chin ordinarily may be removed chemosurgically without noticeable defect (Figs. 28 and 29) Likewise, cancer of the skin of the lower lip may be removed without appreciable defects if the orbicularis oris muscle is not deeply invaded (Fig 30) However neoplasms which have invaded through the muscles into the mucosa usually necessitate defects which require repair for the sake of both ap-

pearance and function. Because of the sureness of removal made possible by the microscopically guided excisions, the repair may be done immediately upon completion of chemosurgical extirpation (Figs. 31 and 32)

to approach these structures rather closely with the chemosurgical technic. This is necessary sometimes because some carcinomas extend medialward around the anterior edge of the sternomastoid muscle to the tissues adjacent



Fig 29 (A) Basal cell carcinoma which had recurred after roentgen therapy (B) Fixed tissue on the third day of chemosurgical treatment. The origin of the five specimens is indicated by marks made with mercurochrome. At this level the carcinoma was confined to the lumens of several lymphatic vessels in the central and inferior portions of specimens 1 2 and 3 The next excised layer was free of cancer (C) Granulation tissue after separation of the final layer of fixed tissue. (D) Healed lesion. There was no recurrence after three years.

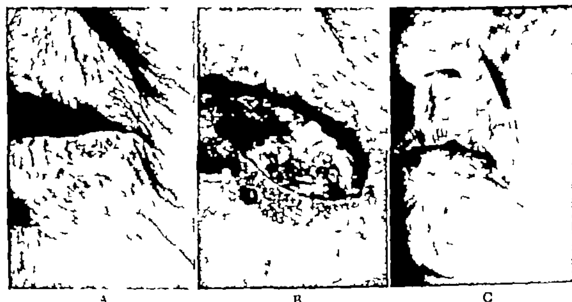


Fig. 30. (A) Basal cell carcinoma which arose just below the vermilion border (B) Granulation tissue after removal of the neoplasm which invaded into the muscle for a short distance. (C) Healed lesion. There was no recurrence after nine years.

Neck

Neoplasms of the neck are amenable to chemosurgical treatment unless there is erosion into such vital structures as the carotid artery or the spinal canal. However it often is possible to the carotid sheath (Figs. 33 and 34) Other cancers may invade deeply just posterior to the sternomastoid muscle (Fig 35) The muscle itself usually is quite resistant to invasion.

The postchemosurgical scars vary in shape

A B C

D

Fig. 31 (A) Basal cell carcinoma, morphea like type Twenty years previously the patient had received roentgen therapy for acne which condition subsequently regressed except for one indurated area in the lower lip. This persisted unchanged for eighteen years and then began slowly to enlarge There was no grossly visible change in the skin except for a slightly yellowish cast. The circle indicates the palpable induration. (B) Fixed tissue after excision of second layer The tissues at this level were full of invasive sclerosing basal cell carcinoma. (C) Granulation tissue in upper half and adherent fixed tissue in lower half of lesion at completion of active chemosurgical treatment. The carcinoma extended well beyond the palpably indurated area and in the center it penetrated the mucosa. (D) Healed lesion immediately after a plastic repair which was carried out without a waiting period by Dr W Slaughter There was no recurrence after five years.



Fig 32 (A) Basal cell carcinoma of a highly invasive sclerosing type. It had recurred after repeated treatments with roentgen rays, radium and liquid nitrogen. In one area there was frank squamous cell carcinoma of relatively recent origin. Both types of neoplasm invaded through the muscle and mucosa to the periosteum of the mandible (B) Granulation tissue and bone after chemosurgical excision. The involvement of the vermilion border necessitated interruption of the continuity of the lip (C) Healed lesion after repair by Dr F Bernard. The repair was delayed until the final layer of fixed bone had separated. There was no recurrence after five years.

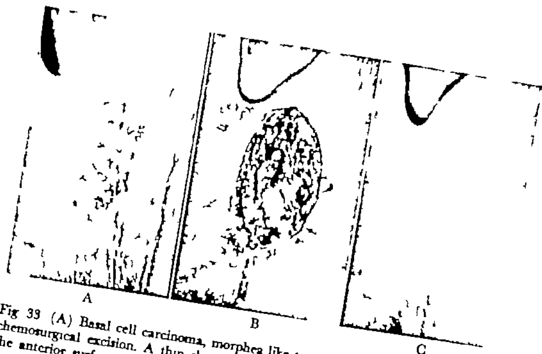


Fig 33 (A) Basal cell carcinoma, morphea like type. (B) Granulation tissue after chemosurgical excision. A thin sheet of cancer tissue extended medialward along the anterior surface of the sternomastoid muscle. (C) Healed lesion showing the linear scar. There was no recurrence after eleven years.

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Fig 34 (A) Squamous cell carcinoma, grade 2, in a nine year old boy with xeroderma pigmentosum. He had developed several cancers, the first at the age of three. For the neoplasm shown here he had recen two courses of roentgen therapy but the mass continued to enlar rapidly (B) Granulation tissue after chemosurgical excision. T cancer extended deeply along the anterior edge of the sternomastoi muscle but did not erode the carotid sheath. (C) Healed lesio Twenty-seven more cancers subsequently were chemosurgically ex cised and at the age of twenty-one he was free of cancer (D) Patient at age twenty

in different areas of the neck. Thus those on the side of the neck usually form a linear scar (Fig 33) while those on the back of the neck may form a linear scar in some patients (Fig 36) but a round scar in others (Fig 37). Even



Fig. 35 (A) Basal cell carcinoma, highly invasive type. (B) Granulation tissue after chemosurgical excision. There was deep invasion between the sternomastoid and trapezius muscles. (C) Healed lesion. There was no recurrence after six years.

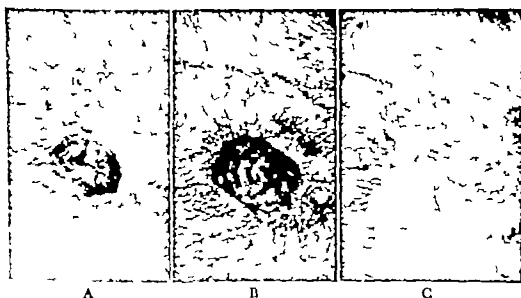


Fig. 36 (A) Squamous cell carcinoma, grade 1 It had recurred after electrodesiccation. (B) Granulation tissue after chemosurgical excision. (C) Healed lesion. The scar is linear There was no recurrence after five years.

large recurrent lesions usually are amenable to chemosurgical treatment and the wounds heal satisfactorily with the formation of soft, smooth, pliable scars (Figs. 37 38 and 39) However in some of such cases grafts may be indicated to speed closure and reduce scar contraction

Therapeutic Results in Cases of Basal Cell Carcinoma of the Face, Scalp and Neck

A total of 461 basal cell carcinomas of the face scalp and neck were chemosurgically excised during the twelve years ending six years prior to the date of this writing The cancers were in all stages from early to far advanced. Over a third of the patients previously had been unsuccessfully treated by operation or irradiation. There were no metastases.



Fig 33 (A) Basal cell carcinoma, morphea-like type (B) Granulation tissue after chemosurgical excision. A thin sheet of cancer tissue extended medialward along the anterior surface of the sternomastoid muscle (C) Healed lesion showing the linear scar There was no recurrence after eleven years.

A B C

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Fig 34 (A) Squamous cell carcinoma, grade 2, in a nine year old boy with xeroderma pigmentosum. He had developed several cancers, the first at the age of three. For the neoplasm shown here he had received two courses of roentgen therapy but the mass continued to enlarge rapidly (B) Granulation tissue after chemosurgical excision. The cancer extended deeply along the anterior edge of the sternomastoid muscle but did not erode the carotid sheath. (C) Healed lesion. Twenty-seven more cancers subsequently were chemosurgically excised and at the age of twenty-one he was free of cancer (D) Patient at age twenty

different areas of the neck. Thus, those on the side of the neck usually form a linear scar (Fig. 33) while those on the back of the neck may form a linear scar in some patients (Fig. 36) but a round scar in others (Fig. 37). Even

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Fig. 35. (A) Basal cell carcinoma, highly invasive type. (B) Granulation tissue after chemosurgical excision. There was deep invasion between the sternomastoid and trapezius muscles. (C) Healed lesion. There was no recurrence after six years.

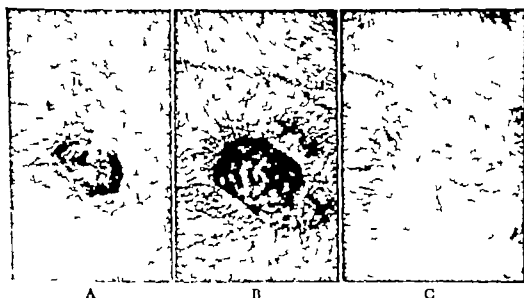


Fig. 36. (A) Squamous cell carcinoma, grade 1. It had recurred after electrodesiccation. (B) Granulation tissue after chemosurgical excision. (C) Healed lesion. The scar is linear. There was no recurrence after five years.

large recurrent lesions usually are amenable to chemosurgical treatment and the wounds heal satisfactorily with the formation of soft, smooth, pliable scars (Figs. 37, 38 and 39). However, in some of such cases grafts may be indicated to speed closure and reduce scar contraction.

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A B C

D

Fig 37 (A) Basal cell carcinoma. It had recurred after radium treatment. (B) Granulation tissue after chemosurgical excision. (C) Reconstruction showing grossly visible cancer (central dark area) grossly palpable induration (light colored ring) and actual extent of the cancer as demonstrated microscopically (entire model). Most of the peripheral extension was in the dermis. (D) Healed lesion. There was no recurrence after five years.



A B C

Fig 38 (A) Squamous cell carcinoma, grade 2, which had arisen in a scar produced by roentgen therapy of toxic goiter twenty three years previously. The neoplasm had recurred after treatment with roentgen rays and caustics. (B) Granulation tissues after chemosurgical excision. The microscopic sections revealed that there was much more invasion of the scar tissue than was anticipated. (C) Healed lesion. The vascularity of the chemosurgical scar was greater than that of the radiation scar. There was no recurrence after six years.

The 464 consecutive cases were divided into "indeterminate" and "determinate" groups. The indeterminate group included the cases of 118 patients who died of intercurrent disease before the expiration of the five year period without evidence of cancer and the cases of eight patients who were lost from observation without evidence of cancer when last seen. The determinate group included the unsuccessfully treated cases of which there were none and the 338 successfully treated cases.

Thus, successful five year end results were

obtained in 100 per cent of the 338 determinate cases of basal cell carcinoma of the face, scalp and neck.

The effect of the size of the lesion on prognosis cannot be expressed in statistical terms on the basis of the present data because the results were uniformly successful regardless of size. However, it is obvious that an advanced basal cell carcinoma with involvement of a vital structure such as the brain or the internal carotid artery might be incurable It happened that none of the 464 lesions of this series had eroded such structures. This is not to say however that the series does not include a considerable number of large lesions. Quite the contrary there are included an unusual proportion of advanced lesions in patients who came from distant points because of the incurability of their lesions with the usual radiation and surgical technics available in their locality

In order to indicate the relative numbers of cancers of various degrees of advancement the 338 cases in the determinate group were divided into four groups according to their average diameter as measured by calipers at the initial clinical examination A, under 1 cm. B 1 to 2 cm. C 2 to 3 cm. and D 3 cm. or more. Examples of basal cell carcinomas in the various classifications are illustrated by the photographs as follows group B in Figures 4 19 20 24 26 30 and 31 group C in Figures 15 22 25 and 29 and group D in Figures 5 6 7 9 11, 13 16, 17 21 32 33 35, 37 and 39 It is apparent from the photographs taken at the completion of treatment that many of the lesions were proved microscopically to be considerably more extensive than the initial clinical examination revealed However to allow comparison with the series of other authors, the initial apparent size rather than the actual size of the neoplasm always was recorded Although 129 lesions were under 1 cm in diameter a greater number were of larger size (Table II)



Fig. 39 (A) Basal cell carcinoma, highly invasive anaplastic type. (B) Granulation tissue after chemosurgical excision. (C) Healed lesion. There was no recurrence after five years.

TABLE II
DISTRIBUTION OF BASAL CELL CARCINOMA OF THE FACE, SCALP AND NECK ACCORDING TO SIZE

Group	Average Diameter Cm.	Number of Lesions
A	under 1	129
B	1 to 2	128
C	2 to 3	46
D	3 or more	35

The effect of previous treatment on prognosis also is not indicated by the present data because all of the patients were successfully treated with chemosurgery regardless of whether or not they had received previous surgical or irradiation treatment. However the fact that 36 4 per cent of the 338 patients in the deter

minate group had recurrent cancers all of which were susceptible to eradication by the chemosurgical technic attests to the efficacy of this method in the treatment of recurrent basal cell carcinomas of the face, scalp and neck. Undoubtedly this unusual success in the treatment of recurrent cancers is largely because of the microscopically controlled technic which makes it possible to follow out residual foci which otherwise might be obscured by scar tissue.

Although there were no unsuccessfully treated patients in this particular series it must not be concluded that the circumstance of previous unsuccessful treatment is not an unfavorable prognostic factor. There is always the possibility that isolated, outlying foci of cancer might result either from surgical or radiation treatment. Being disconnected from the main mass of cancer these foci might be missed despite the microscopic control afforded by the chemosurgical technic.

The effect of histologic degree of invasiveness on prognosis also is not indicated by the data here presented because all of the basal cell carcinomas of the face, scalp and neck were successfully treated regardless of histopathologic differences. However, the more highly invasive, rodent ulcer type of basal cell carcinoma ordinarily is considered to be a more difficult lesion to eradicate than the nodular type with its relatively low degree of invasiveness. For this reason the cancers have been placed in two groups: one in which invasiveness is high and one in which invasiveness is low. In this series there was a high degree of invasiveness in 64.5 per cent of the cases. The high rate of cure which was attained despite the high degree of invasiveness must be credited to the microscopic control which made it possible to follow out the slender invasive strands as readily as the thicker outgrowths from the less invasive cancers. Some degree of keratinization was observed in 44 (13 per cent) of the basal cell carcinomas and pigmentation was observed in 5 (1.5 per cent) but since keratinization and pigmentation did not alter the response to chemosurgical treatment, no separate classification was provided.

The effect of the site of origin on prognosis again is not indicated by the present data because all of the carcinomas were successfully treated regardless of location. However it is obvious that lesions located over vital structures such as the brain or large vessels of the neck would potentially be more dangerous than those not so situated. The incidence of basal cell carcinoma in the various sites is tabulated herewith in order of decreasing frequency (Table III).

TABLE III
DISTRIBUTION ACCORDING TO SITE OF ORIGIN OF BASAL CELL CARCINOMAS OF THE FACE, SCALP AND NECK

Site	*Number of Lesions*
Cheek	165
Temple	42
Forehead	34
Upper lip (skin)	35
Neck	25
Chin and skin of lower lip	21
Scalp	16

Therapeutic Results in Cases of Squamous Cell Carcinoma of the Face, Scalp and Neck

Altogether 230 squamous cell carcinomas of the face, scalp and neck were excised chemosurgically during the twelve years ending six years prior to the date of this writing. The cancers ranged in extent from very early to far advanced. One fourth of the patients had received previous unsuccessful radiation or surgical treatment. Metastasis in the regional lymph nodes was present in nineteen cases.

The 230 consecutive cases were divided into indeterminate and determinate groups (Table IV). The indeterminate group included the cases of sixty five patients who died of intercurrent disease before the expiration of the five year period without evidence of cancer and the case of one patient who was lost from observation without evidence of cancer when last seen. The determinate group included 164 cases made up of the unsuccessful results of which there were twenty five and the successful results of which there were 139.

Therefore, after observation periods of five years or more, successful results were obtained in 84.8 per cent of the 164 cases of squamous cell carcinoma in this group. A considerable proportion of the unsuccessful results were the result of metastases as indicated by the fact that

TABLE IV

FIVE-YEAR END RESULTS SQUAMOUS CELL CARCINOMA OF THE FACE, SCALP AND NECK

This series includes the cases of all patients with histologically proved squamous cell carcinoma, both early and advanced, previously untreated and recurrent with and without metastasis, who were chemosurgically treated during the twelve year period ending six years prior to this writing

Total number of cases	230
Indeterminate group, total number	66
Patients dead from other causes without recurrence	65
Patients lost from observation without recurrence	1
Determinate group, total number	164
Unsuccessful results, total number	25
Patients dead, cancer present at death	19
Patients lost from observation with cancer	6
Patients living with cancer	0
Successful results, patients free of cancer for five years or more	139
Five-year rate of cure (139 + 164) × 100	84 8%

92 1 per cent of the primary lesions were eradicated.

The effect of the size of the lesion on prognosis was appreciable because the larger the neoplasm the greater the chance of invasion of vital structures and the more frequent the occurrence of metastasis Thus, while squamous cell carcinomas of group A (under 1 cm) and group B (1 to 2 cm.) were successfully treated in 100 per cent of the cases, the cure rate dropped precipitously in groups C (2 to 3 cm.) and D (3 cm. or more) to 83.3 per cent and 37 1 per cent respectively (Table V) Examples

TABLE V

EFFECT OF SIZE OF SQUAMOUS CELL CARCINOMA OF THE FACE NECK AND SCALP ON FIVE-YEAR END RESULTS

Group	Average Diameter Cm	Number of Lesions	Successful Results Number	Per cent
A	under 1	61	61	100 0
B	1 to 2	50	50	100 0
C	2 to 3	18	15	83 3
D	3 or more	35	13	37 1

of squamous cell carcinomas in the four groups are as follows group B in Figures 27 28 and 36 group C, in Figure 18 and group D in Figures 8 10 12 14 23 34 and 38

An analysis of the cases in which treatment was unsuccessful serves to indicate the complications which may arise in connection with squamous cell carcinomas of large size. Thus, in this series there was a total of twenty five unsuccessfully treated patients. In seventeen of these in whom the essential cause of failure was uncontrollable regional metastasis the lesions were classified in group D in thirteen cases and group C in four cases Obviously, the larger the lesion the greater was the chance of failure because of metastasis. The rest of the unsuccessfully treated patients all had large carcinomas which were classified in group D In six cases the cause of failure was excessive involvement of vital areas of cerebral tissues in one of these death occurred during treatment but in the other five treatment was discontinued to avoid an immediately fatal outcome. In one case the cause of failure was the presence of widespread embolic foci in the skin lymphatics and in another the cause of failure was local recurrence which could not be treated adequately because the patient was severely incapacitated by a stroke which caused death several months later

Although there is no doubt but that large size is an unfavorable prognostic factor it is to be stressed that size in itself is no barrier to cure by means of chemosurgery It is only when the large size leads to complications such as metastasis or invasion of vital structures that the prognosis becomes poor It is significant that a considerable number of extremely advanced squamous cell carcinomas were eradicated by chemosurgical treatment.

The effect of previous treatment on prognosis is definitely adverse as indicated by the comparison of the rate of cure of 59.5 per cent for the group of forty two patients who had received previous treatment with the rate of 93 4 per cent for the group of 122 patients who had not received previous treatment

The adverse effect of previous unsuccessful surgical or radiation treatment is mainly because of the delay occasioned by these procedures This delay tends to allow more time for the invasion of vital structures and for the occurrence of metastasis. In some cases moreover there was evidence that the carcinoma had been spread into the surrounding tissues during surgical excision and in other cases there was a considerable increase in the grade

of malignancy following prolonged radiation therapy Both of these factors, in addition to the delay served to decrease the chance of cure by chemosurgical treatment. However the fact that over half of the patients whose cancers had not responded to surgical or radiation treatment were cured by means of the chemosurgical technic indicates that this method is of distinct value in the treatment of recurrent cancer

The effect of the histologic grade of malignancy on prognosis is significant as indicated by the drop in the rate of cure from 94 6 per cent for grade 1 squamous cell carcinoma to 30 per cent for grade 4 carcinoma (Table VI) Fortunately two-thirds of the neoplasms came under the classification of grade 1 or grade 2 Broders classification was used

TABLE VI

EFFECT OF HISTOLOGIC GRADE OF MALIGNANCY OF SQUAMOUS CELL CARCINOMA OF THE FACE, SCALP AND NECK ON FIVE-YEAR END RESULTS

Grade	*Number of Lesions*	*Successful Results*	
		Number	*Per cent*
1	37	35	94 6
2	78	73	93 6
3	39	28	71 8
4	10	3	30 0

The danger of metastasis and of earlier invasion of vital structures such as the brain or large vessels of the neck accounts for the impaired prognosis with increasing degrees of malignancy Otherwise there would be little difference in the rate of cure because the chemosurgical technic is just as effective in following out slender highly invasive strands of grade 4 carcinoma as it is in tracing the more lobular outgrowths of grade 1 carcinoma. As a matter of fact the need for chemosurgical treatment is particularly great in cases of highly invasive neoplasms which tend to send out "silent" extensions which otherwise might go unrecognized.

The effect of site of origin on prognosis of squamous cell carcinoma is relatively minor despite the data given herewith (Table VII) The lowest rate of cure (50 per cent) was for carcinoma of the forehead and the next lowest (75 per cent) was for the scalp. Actually lesions in these areas are not as dangerous as these data would suggest it just happened that most of the forehead and scalp cancers in this series were very advanced Thus, of the six unsuccessfully treated patients with forehead lesions three had metastases and three had too much involvement of the dura for a cure to be attained. One of the scalp lesions also extensively involved the dura. Actually one would expect carcinoma of the neck to be dangerous because of the possibility of involvement of the common or internal carotid artery but it so happened that only one patient in this group was unsuccessfully treated and this failure was due to metastasis rather than to involvement of vessels or other vital structures. As would be expected lesions affecting the cheek, temple and upper lip were successfully treated in a high proportion of the cases because of the relative lack of underlying vital structures. Two of the five chin lesions exhibited a strong tendency to spread in the superficial lymphatic vessels with the formation of satellite skin nodules, and because these foci were not connected with the main neoplasm their presence was not always detected by the microscopically guided excisions. Fortunately the incidence of this phenomenon is only approximately one in 400 cases of squamous cell carcinoma of the skin.

TABLE VII

EFFECT OF SITE OF ORIGIN OF SQUAMOUS CELL CARCINOMA OF THE FACE, SCALP AND NECK ON FIVE-YEAR END RESULTS

Site	*Number of Lesions*	*Successful Results*	
		Number	*Per cent*
Cheek	84	72	85 7
Temple	29	26	89 7
Forehead	12	6	50 0
Upper lip (skin)	6	5	83 3
Neck	23	22	95 7
Chin	6	5	83 3
Scalp	4	3	75 0
All sites	164	139	84 8

The effect of metastasis on prognosis of squamous cell carcinoma is considerable. Thus, in all of the nineteen cases in which metastasis had occurred the outcome was fatal while in the 145 cases in which there was no metastasis

the five-year cure rate was 95.9 per cent. Actually, metastasis should not be as potent an adverse factor as these data indicate. There were extenuating circumstances in this series. Many of the patients were in poor general condition, some had hopelessly extensive cervical metastasis, one had leukemia, and others refused the recommended dissections. Only nine of the nineteen cases were amenable to resection and of these several should have had more radical dissections as subsequent events proved. Palliative roentgen therapy was given in several cases.

In a reasonably healthy patient with metastatic nodes of reasonable size there should be a good chance of cure by a thorough dissection of the node-bearing areas. Prophylactic dissection of nodes was carried out in only one case in this series, yet the patient died of metastasis. However, in cases with large primary carcinomas of a fairly high grade of malignancy located in an area with readily accessible regional nodes, prophylactic dissections usually are advisable.

Comparison of Results with Those of Other Authors

There are a few series in the literature that are large enough and sufficiently adequate as regards follow up and statistical evaluation to serve as a basis for comparison with the results obtained with the chemosurgical treatment of cancer of the face, scalp and neck. One of the best series with respect to both statistical validity and also excellent therapeutic results is that of Magnussen[41] who reported on the results obtained with the highly developed radiologic, surgical and electrosurgical technics employed at Radiumhemmet in Stockholm, Sweden. Therefore, his data is used extensively for comparison.

From Magnussen's protocols it was determined that in his series of 101 cases of basal cell carcinoma of the face, scalp and neck his five year rate of cure was 93.1 per cent while in the present series of 338 determinate cases in which chemosurgical treatment was used the rate of cure was 100 per cent. The distribution of lesions of various sizes in the two series was not greatly different (30.3 per cent in groups C and D in Magnussen's series and 24 per cent in the present series) and the proportion of patients who had received previous unsuccessful treatment also was of the same order (26.7 per cent in Magnussen's series and 36.4 per cent in the present series).

In Magnussen's series of forty-five cases of squamous cell carcinoma of the face, scalp and neck, the five-year cure rate was 64.4 per cent while in the present series of 164 cases in which chemosurgical treatment was used the rate of cure was 84.8 per cent. However, the sizes of the lesions in Magnussen's series were larger (56.8 per cent in groups C and D as compared to 33.5 per cent in the present series). Previous unsuccessful treatment had been received by 22.2 per cent of Magnussen's patients and by 25.6 per cent of the patients in this series.

These data indicate that the therapeutic results obtained with the chemosurgical method are better than the best reported results obtained with the usual radiologic and surgical methods. The microscopic control of excision afforded by the chemosurgical technic is responsible for this unprecedented reliability and also for the relatively conservative approach. Moreover, in this series of 694 cases of cancer of the face, scalp and neck there was only one death attributable to chemosurgical treatment; this occurred in a patient with extensive carcinomatous invasion of the dura and frontal lobe of the brain.

CHAPTER 4

Carcinoma of the Nose

THE microscopic control of excision afforded by the chemosurgical technic is of particular value in the treatment of nasal carcinomas because these neoplasms often exhibit ramifications which cannot be predicted clinically[34] The reasons why these extensions are unpredictable are twofold First, cancer tissue has much the same consistency as the fibrocartilaginous tissue of the nose making it difficult to distinguish one from the other by palpation. Second, cancer of the nose often invades in a surprisingly irregular and unpredictable manner through tissues such as dermis, periosteum, perichondrium perineurium, lymphatic vessels and embryologic fusion planes which structures have a reduced resistance to the spread of some cancers. This tendency is particularly striking in the tissues of the nasolabial fold, the alae the root of the nose near the inner canthi and the septum but it also often is observed in other parts of the nose These extensions frequently take the form of slender infiltrating strands which are undetectable except by means of the microscope

Cancers of the various parts of the nose present different therapeutic problems therefore, they are considered separately under the following headings root, bridge, tip, alae, nasolabial fold and septum The therapeutic results in cases of basal cell and squamous cell carcinoma are presented at the end of the chapter

Root

Though the deep spread of carcinoma of the root of the nose is effectively limited by the underlying nasal bone the peripheral spread is met with no barriers. Hence there is ready extension into the forehead, the nasal bridge and the inner canthal regions. Involvement of forehead, eyebrow and upper eyelid tissues can be rather extensive without precluding a satisfactory cosmetic and functional result upon chemosurgical treatment (Fig 40) Healing is favorable since these rather elastic tissues stretch across the underlying bony framework to form a smooth, soft, pliable scar which soon assumes approximately the same color as the surrounding skin. Plastic repairs rarely are necessary Carcinomas in the middle of the root often show some tendency to send out slender invasive strands into the softer tissues of the inner canthal regions. Fortunately these extensions tend to remain close to the medial wall of the orbit as they extend posteriorly therefore, the eyeball and the extraocular muscles usually are not invaded. Not infrequently the lacrimal sac is involved and at times the carcinoma extends downward in the lacrimal fossa. There can be considerable involvement of inner canthal structures, however without there being produced appreciable functional or cosmetic defect upon chemosurgical treatment (Fig 41) Even small lesions may show a tendency to invade the inner canthal tissues more than in other directions (Fig 42) but in the individual case there is no way to predict in which direction the grossly invisible extensions will grow

Because of the thinness of the tissues over the nasal bone the periosteum often is involved. When the periosteum is removed there necessarily is destroyed a thin layer of nasal bone. Care should be exercised not to apply much fixative to the bone because this might result in an unnecessary defect through the mucosa. The fixed bone becomes demarcated from the underlying viable bone after two to three weeks when it may be lifted off with a rongeur or forceps. The fixed soft tissues usually separate from this area in about seven days.

Carcinomatous invasion through the bone into the ethmoid sinuses is not a serious com-

A B C

D

Fig 40 (A) Basal cell carcinoma which had recurred after electrodesiccation, surgical excision and three courses of roentgen therapy. The mark on the skin indicates the extent of palpable induration (B) Lesion at completion of chemosurgical excision showing the fixed tissue still in place. The carcinoma extended farther than expected into the forehead and into both inner canthi (C) Granulation tissue with exposed nasal and frontal bones in the center. This was seven days after the last chemosurgical excision. (D) Healed lesion. There was no recurrence when the patient died of other causes after three years.



Fig 41 (A) Basal cell carcinoma which had recurred after electrodesiccation and radium treatment (B) Granulation tissue and exposed nasal bone after chemosurgical excision. The highly invasive cancer had extended for an unexpected distance into the forehead and into both canthi (C) Healed lesion. There was no cosmetic or functional defect in the canthi. There was no recurrence after five years.



Fig 42 (A) Basal cell carcinoma. (B) Granulation tissue after chemosurgical excision There was more extension into the inner canthus than was predicted clinically (C) Healed lesion. There was no recurrence after five years.

plication unless the neoplasm has eroded to the region of the cribriform plate. Great care must be used lest this bone be penetrated by the fixative because fatal encephalomalacia readily may be produced. There is often some difficulty in properly sectioning the tissues from the ethmoid air cells because of the many paper thin bones, but it can be done by carefully removing the bony spicules before frozen sections are made.

Bridge

The osseous and cartilaginous framework of the nasal bridge has much to do with the depth to which carcinomas may spread in this area. Thus, in the upper bridge the nasal bone provides a strong barrier to deep spread while in the lower bridge the lateral and greater alar cartilages provide a definite but considerably weaker barrier Often the deeper extensions permeate through the clefts between the cartilages. A frequent point of deep spread is in the midline where the lateral and greater alar cartilages appose the septal cartilage (Fig 43)

The conservatism which is inherent in the chemosurgical method makes it possible to avoid defects through the mucosa if this membrane is not actually involved. With the outgrowing nodular type of basal cell carcinoma treatment often can be very conservative. However with the ingrowing invasive type, the excision often must be considerably more radical than would have been expected from the initial appearance of the lesion. Sometimes the unexpected spread is predominantly at the periphery (Fig 44) sometimes it is in the center (Fig 45) but most commonly it is in both areas. (Fig 46) In any event, it is necessary to be well acquainted with the anatomy of the nose and to use meticulous care in chemosurgical treatment to avoid unnecessary penetration of the mucosa.

Advanced lesions with cancerous invasion of the mucosa necessitate defects through the nasal wall, but the size of the defects may be kept at a minimum by the chemosurgical method of treatment. Not infrequently the carcinoma must be followed posteriorly along the septum or along the mucosa of the lateral nasal wall and of the turbinates (Figs. 47 and 48) More advanced lesions may extend considerably beyond the nasal bridge and yet be amenable to chemosurgical treatment (Fig 49) No matter how radical the excision may have to be, excision is as conservative as the actual extent of the neoplasm will permit hence, the plastic repair of the defect is less formidable than it would be after surgical excision in which a wide margin of normal tissue must be removed to provide reasonable assurance of complete eradication of the cancer



Fig. 43 (A) Basal cell carcinoma which had recurred after roentgen ray and radium treatment. (B) Granulation tissue after chemosurgical excision. Deep extension of the cancer plus atrophy from previous irradiation necessitated removal of portions of nasal bone, cartilages and mucosa. (C) Healed lesion after two years. The hole into the mucosa closed completely several months later. Ordinarily such a defect would be repaired at an early date. There was no recurrence after twelve years.



Fig. 44 (A) Basal cell carcinoma which had been treated with roentgen rays and which showed evidence of recurrence in three places. (B) Granulation tissue after chemosurgical excision which revealed carcinoma under the entire scar and in the dermis at the periphery especially at the superior edge. (C) Healed lesion. There was no recurrence after six years.

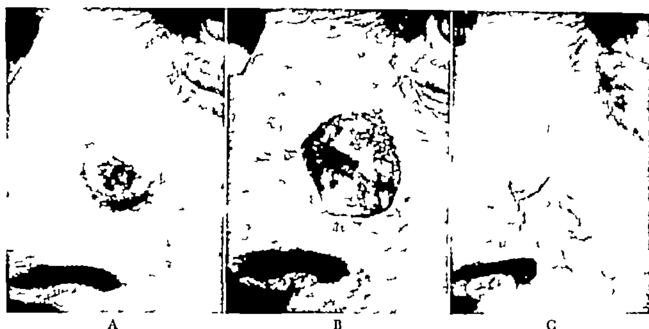


Fig 45 (A) Squamous cell carcinoma, grade 3 malignancy (B) Granulation tissue after chemosurgical excision. The frozen sections from the deepest level revealed cancer among the mucosal glands but the mucosa itself was not invaded and hence was preserved. (C) Healed lesion. There was no recurrence after nine years.

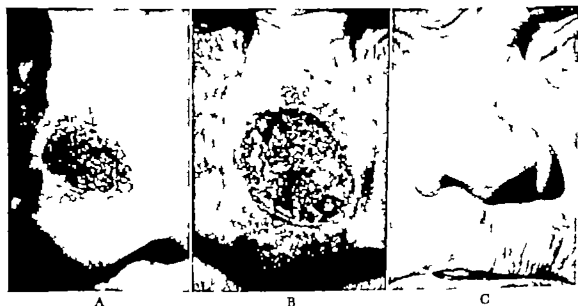


Fig 46 (A) Basal cell carcinoma. (B) Granulation tissue after chemosurgical excision of the highly invasive cancer which spread more widely and deeply than expected. (C) Healed lesion. There was no recurrence after six years.



Fig 47 (A) Originally basal cell carcinoma but with squamous cell component of relatively recent onset. This change in cell type may have been produced by the thirty radium treatments received over a period of three years (B) Granulation tissue after chemosurgical excision. The mass had protruded into the nasal cavity and there had been invasion between the mucosa and cartilages of the septum and of the nasal bridge (C) Healed lesion just before the plastic repair There was no recurrence after five years.

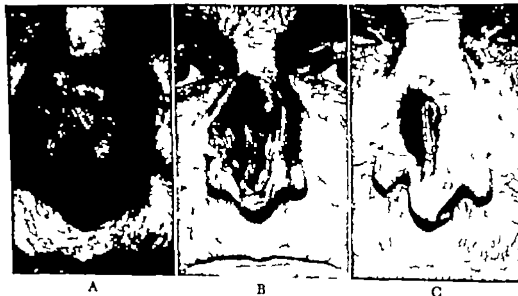


Fig 48 (A) Squamous cell carcinoma, grade 2 malignancy The neoplasm had grown to this size in three months. Three small roentgen ray treatments had been given in the belief that the lesion was an inflammatory process. (B) Granulation tissue after chemosurgical excision. The preservation of the rima nasi makes possible a more satisfactory repair (C) Healed lesion before repair There was no recurrence when he died of other causes after two and one-half years.

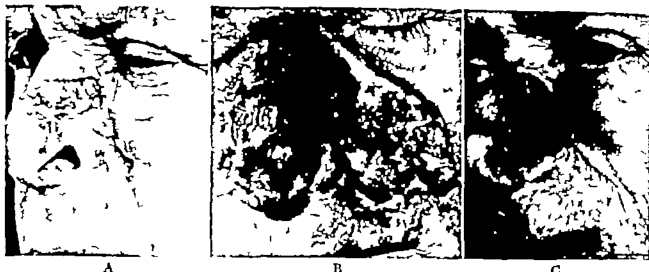


Fig. 49 (A) Basal cell carcinoma which had recurred after treatment at a well known cancer center by means of electrodesiccation, radium placques, roentgen rays, radon seeds, and surgical excision with plastic repair (B) Granulation tissue after chemosurgical excision. The highly invasive basal cell carcinoma invaded much of the bridge and left ala but extended much farther than expected in the root, in the septum and in the left cheek. (C) Healed lesion just prior to repair There was no recurrence after twelve years.

Tip

If not too advanced, carcinomas of the tip of the nose can be chemosurgically excised without appreciable defect (Fig 50) However if the carcinoma involves the full thickness there will result a hole (Fig 51) or a niche (Fig 52) which may require a repair When there is a loss of cartilage the wound may heal with the formation of a depression but this fills in to some extent after several months (Fig 53) Neglected neoplasms may destroy the entire nose and if this occurs in elderly patients a prosthesis often is preferred rather than a plastic repair (Fig 54)

Irregular extensions are common, particularly in the clefts between the greater alar cartilages and the septal cartilage. Familiarity with the disposition of these cartilages and care in following the extensions with repeated thorough microscopic checks on progress are essential factors in the avoidance of unnecessary defects. If repairs are necessary the certainty of complete eradication of the cancer often justifies immediate rather than delayed procedures.

Occasionally during the chemosurgical treatment of neoplasms of the bridge or tip arteries with appreciable pressure are encountered. These often require the insertion of suture ligatures at the completion of active chemosurgical treatment in order to avoid the possibility of hemorrhage during the separation of the final layer of fixed tissue.

Alae

A majority of cancers of the nasal alae are of the highly invasive type of basal cell carcinoma which infiltrates the nasal tissue without producing much of a protruding mass. Hence, the neoplasms often are found to have spread farther than suggested by the clinical appearance of the lesion (Fig 55) This unpredictability of the extent of many alar lesions doubtless explains why there sometimes may be recurrence following supposedly adequate radiation (Fig 56) or surgical treatment (Fig 57)

Many alar lesions are removed chemosurgically without prior surgical excision because the swelling produced by the initial chemical treatment provides an extra margin of safety However with proper care, preliminary surgical removal gives good results with appreciable saving of time and discomfort (Fig. 58)

Because of the conservatism of the chemosurgical treatment of alar lesions the defects are kept at a minimum. Therefore often it is possible to avoid the necessity of a plastic repair but if not, the relatively small defect can be repaired more easily and more satisfactorily than can a large one. For example, cancers ex

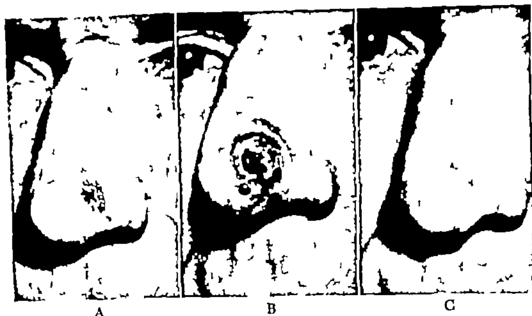


Fig 50 (A) Basal cell carcinoma which has recurred after roentgen therapy (B) Granulation tissue after chemosurgical excision. The carcinoma extended to the greater alar cartilage and necessitated removal of a piece 8 mm. in diameter (C) Healed lesion. There was no recurrence after five years.



Fig 51 (A) Squamous cell carcinoma, grade 3 malignancy It had recurred after radium treatments. (B) Granulation tissue and 3 × 6 mm. defect through the mucosa. (C) Healed lesion. The hole had closed spontaneously to less than 1 mm. in diameter There was no recurrence after four years.

tending through the entire thickness of the superior portions of the alae often can be removed without the loss of the nasal rim which is difficult to repair perfectly when the defect is large Even if it is necessary to produce a defect in the rim, it may be kept so small that relatively minor procedures such as the transplant of a small free graft from the helix of the ear may be feasible.

The fixative chemical tends to penetrate rather readily through alar tissues for three reasons (1) the alae are relatively non-expansile (2) the blood supply to the mid portion of the alae is readily compromised by the action of the fixative on the proximal or distal portions, and (3) the alae are small confined structures which cannot dissipate much fixative. Because of this ready penetration, care must be used to avoid overdosage with consequent unnecessary defects.

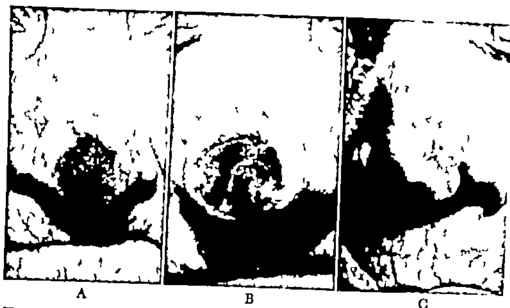


Fig 52 (A) Basal cell carcinoma (B) Granulation tissue after chemosurgical excision (C) Healed lesion. A repair was not urged upon the patient because of his age of eighty-three. There was no recurrence after five years.

Fig 53 (A) Basal cell carcinoma which had recurred after electrodesiccation on nine occasions. (B) Fixed tissue at completion of chemosurgical excision. The excised specimens and the frozen sections are to the left. (C) Granulation tissue The removed final layer of fixed tissue including a piece of cartilage are to the left. (D) Healed lesion after two months. This depression flattened out gradually during the next few months. There was no recurrence when the patient died of other causes after ten years.

A B C

D

Fig 54 (A) Squamous cell carcinoma, grade 1 malignancy There was a metastatic nodule in an outlying lymphatic vessel of the skin in the left inner canthal area. (B) Healed lesion after chemosurgical excision of the primary and metastatic lesions. (C) Photomicrograph showing appearance of tissue fixed in situ with zinc chloride (lower ⅔) as compared to the tissue fixed in vitro with Bouin's solution (upper ⅓) (D) Prosthesis which was preferable to a repair because the patient was ninety-one years old. There was no recurrence after five years.



Fig 55 (A) Basal cell carcinoma. (B) Lesion during treatment. The fixative (black) has been applied to a microscopically demonstrated extension of carcinoma in the dermis at the upper medial edge (C) Healed lesion. There was no recurrence after four years.



Fig. 56 (*A*) Squamous cell carcinoma, grade 3 which had recurred after roentgen therapy twelve radium treatments and three electrodesiccation treatments (B) Granulation tissue after chemosurgical excision. The cancer extended through the mucosa and for a considerable distance superiorly and medially However the root of the nasal ala was spared (C) Healed lesion just before plastic repair There was no recurrence after eight years.

A B C

D

Fig. 57 (A) Basal cell carcinoma which had recurred after excision. (B) Lesion during treatment. Marks with mercurochrome show the origin of each of five specimens of fixed tissue. The second area from the left was the only one which contained cancer at this level (C) Granulation tissue three days later Fixed tissue adheres to the area which received the last application of fixative. (D) Healed lesion before repair There was no recurrence after six years.

Fig 58 (*Opposite*) Photographs showing stages of surgical and chemosurgical treatment. (A) Squamous cell carcinoma, grade 1 (B) Lesion immediately after cold knife excision and hemostasis with dichloracetic acid. (C) Whitened peripheral skin after application of dichloracetic acid. (D) Application of the zinc chloride fixative paste. (E) Lesion after the first chemosurgical excision, three hours after the application of the fixative. The specimens of fixed tissue are to the left and the frozen sections are to the right of the lesion. Above is a map showing the origin of the three specimens and the location of the residual carcinoma (shaded area) The fixative has been reapplied to the cancerous area. One hour later another layer was excised from the latter area. The sections revealed an area of cancer 2 mm. in diameter

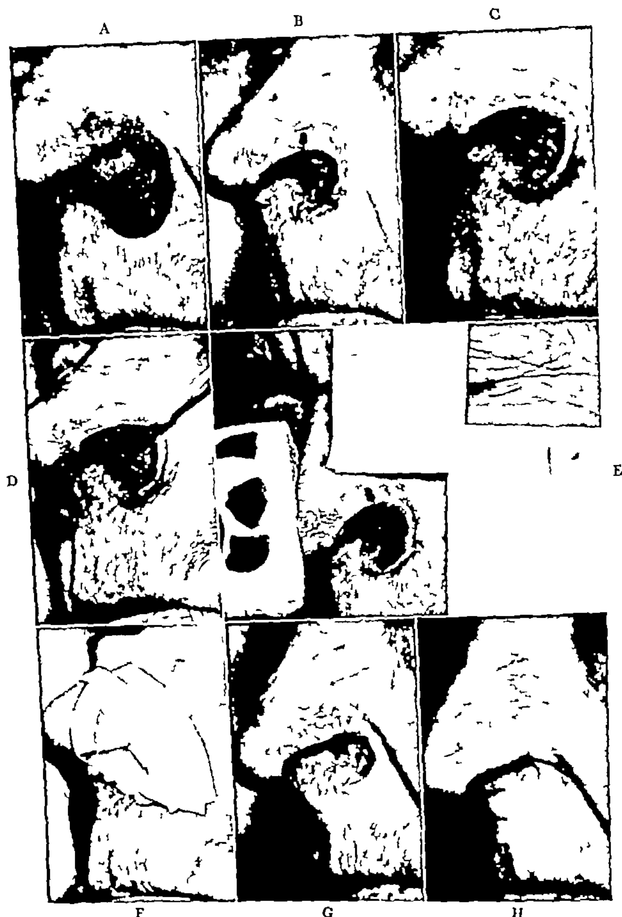


Fig. 38 (*Cont.*)—Another specimen removed a half hour later was free of cancer. The out patient procedure was completed in less than five hours. (F) Dressing to hold fixative in place. (G) Granulation tissue after seven days. The fixed tissue had separated spontaneously. (H) Healed lesion. There was no recurrence after one and one-half years.






Fig 59 (A) Basal cell carcinoma which had recurred after three electrodesiccation treatments and approximately fifty roentgen ray treatments over a period of six years. (B) Granulation tissue after chemosurgical excision. Although the cancer appeared to be localized around the hole through the nose in the nasolabial fold, it actually extensively invaded the ala, the bridge and the embryologic fusion plane. It extended to the tissues on both the medial and lateral sides of the *lower edge of the nasal bone.* (C) *Healed lesion.* (D) Lesion after plastic repair by Dr V B Hyslop There was no recurrence after twelve years.

Nasolabial Fold

Cancer in the region of the nasolabial fold generally is reputed to constitute a troublesome therapeutic problem, especially if it has been neglected or if it has recurred after surgical or radiation treatment. This reputation largely stems from the fact that many neoplasms of this area are highly invasive and tend to send out slender extensions into the surrounding tissues, particularly into the embryologic fusion plane between the nasal and labial anlagen (Fig. 59) These extensions are difficult to differentiate clinically from the normal nasal tissues. Hence the microscopic control of excision provided by the chemosurgical technic is invaluable in assuring complete removal without the necessity of removing large amounts of uninvaded normal tissues (Fig. 60)

Lesions which are not too extensive may be excised chemosurgically without appreciable defect (Fig 61) but some lesions extend for a surprisingly great distance beyond the clinically detectable extent (Fig 62) Advanced lesions may extensively invade the nose and the surrounding tissues (Fig 63) but rarely is the lesion too extensive for eradication by the chemosurgical method

Septum

Carcinoma of the septum is uncommon and is usually of the squamous type. Often the neoplasms exhibit vigorous growth and invasion. If chemosurgical treatment is instituted relatively early the deformity is minimal (Fig 64) but if not there may be considerable destruction (Fig 65)

The technic for keeping the fixative in place on the septum is much the same as elsewhere except that the dressings are held in place by packing the nares with cotton on which petrolatum has been spread. This packing serves not only to hold the dressing in place but also to prevent drying of the fixative by the passage of the inspired and expired air Another technical detail which is useful in the treatment of intranasal lesions is the application of pieces of fixative impregnated gauze over the applied fixative to reduce the tendency for the chemical

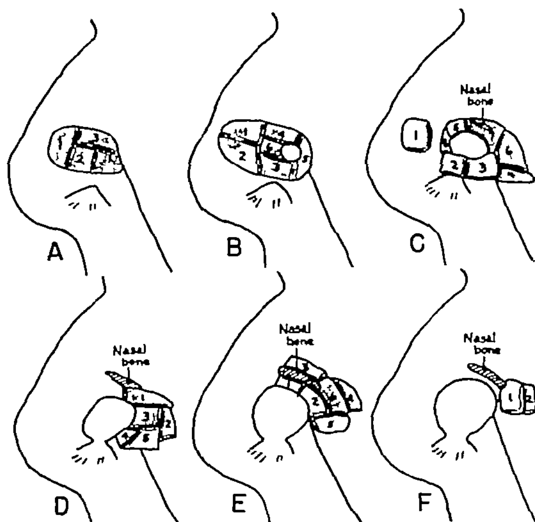


Fig 60 Maps from the case illustrated in figure fifty nine showing the origin of the specimens which were removed by six successive excisions. While it often is possible to surgically remove the grossly visible portion of the cancer prior to chemosurgical treatment the deceptive nature of this neoplasm necessitated the use of microscopically guided chemosurgical excisions throughout.

to be diluted and washed off by the nasal secretions. Double thickness petrolatum gauze to wall off the area under chemosurgical treatment is freely used for the dual purpose of preventing entrance of mucous secretions and of preventing excessive drying. Lesions arising in the vestibule and on the septum above the columella are rare but they too may be chemosurgically treated by the use of packing to keep the dressing in place over the applied fixative



Fig 61 (A) Keratinizing basal cell carcinoma which had recurred after electrodesiccation and radium treatment. (B) Granulation tissue after chemosurgical excision. (C) Healed lesion. There was no recurrence after four years.



Fig 62 (A) Basal cell carcinoma which had recurred after treatment with caustics, electrodesiccation, roentgen rays, radium and surgical excision. (B) Granulation tissue after chemosurgical excision. The cancer invaded for a surprisingly great distance on the cheek and the nasal bridge. (C) Healed lesion after repair by Dr C L. Straith. There was no recurrence after six years.

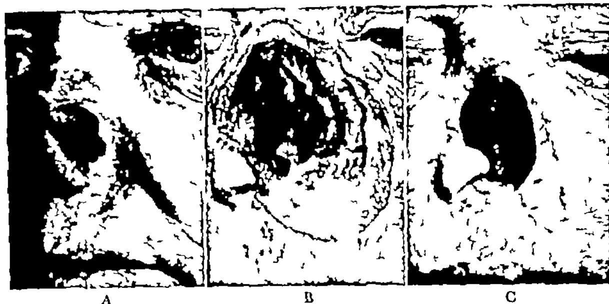


Fig 63 (A) Basal cell carcinoma which had recurred after freezing, electrodessication, roentgen rays and radium treatment. (B) Granulation tissue after chemosurgical excision The septum, turbinates and all walls of the nasal cavity were invaded. (C) Healed lesion before plastic reconstruction of nose. There was no recurrence after nine years.

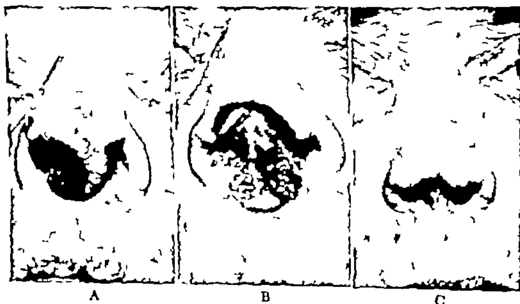


Fig 64 (A) Squamous cell carcinoma, grade 1 malignancy It first was noticed two months previously (B) Granulation tissue after chemosurgical excision. (C) *Healed* lesion. There was no recurrence after five years.



Fig 65 (A) Squamous cell carcinoma, grade 2 malignancy It was first noticed nine months previously (B) Lesion on the fifth day of chemosurgical treatment. (C) Lesion on the fourteenth day of treatment when the last of the cancer was found microscopically (D) Lesion on the sixteenth day just after separation of the final layer of fixed tissue. The cancer had invaded the skin of the tip and bridge but had spared the alae. (E) Lesion after simple closure by Dr W Slaughter The patient had refused reconstruction because of his advanced age. There was no recurrence after five years.

Therapeutic Results in Cases of Basal Cell Carcinoma of the Nose

A total of 308 basal cell carcinomas of the nose were chemosurgically excised during the twelve years ending six years prior to the date of this writing The cancers were in all stages from early to advanced. Forty-one per cent of the patients previously had been unsuccessfully treated by operation or radiation There were no metastases.

The 308 consecutive cases were divided into "determinate" and "indeterminate" groups. The indeterminate group included the cases of eighty two patients who died of intercurrent disease, but without cancer before the expiration of the five year period and the cases of nine patients who were lost from observation without evidence of cancer when last seen. The determinate group included the cases of five unsuccessfully treated patients and the cases of 212 successfully treated patients.

Thus, successful five year end results were obtained in 97 7 per cent of the determinate cases of basal cell carcinoma of the nose (Table VIII)

The effect of the size of the lesion on prognosis is relatively slight until the carcinoma exceeds 3 cm. in diameter This is indicated by the

TABLE VIII

FIVE-YEAR END RESULTS BASAL CELL CARCINOMA OF THE NOSE

This series includes the cases of all patients with histologically proved basal cell carcinoma, both early and advanced, previously untreated and recurrent who were chemosurgically treated during the twelve year period ending six years prior to this writing

Total number of cases	308
Indeterminate group total number	91
Patients dead from other causes without recurrence	82
Patients lost from observation without recurrence	9
Determinate group total number	217
Unsuccessful results, total number	5
Patients dead, cancer present at death	5
Patients lost from observation with cancer	0
Patients living with cancer	0
Successful results, patients free of cancer for five years or more	212
Five-year rate of cure (212 ÷ 217) × 100	97 7%

fact that all of the patients with basal cell carcinoma of less than that size were cured However when the size exceeded 3 cm., the rate of cure dropped to 76 2 per cent (Table IX) In each case the size refers to the average diameter of the lesion as measured with calipers at the initial clinical examination. Examples of basal cell carcinomas of various sizes are as follows group A (diameter under 1 cm.) in Figure 53 group B (diameter 1 to 2 cm.) in Figures 42 44 46 50 55 and 61 group C (diameter 2 to 3 cm.) in Figures 43 52 57 58 59 and 62 and group D (diameter 3 cm. or more) in Figures 40 41 47 49 and 63

TABLE IX

EFFECT OF SIZE OF BASAL CELL CARCINOMA OF THE NOSE ON FIVE-YEAR END RESULTS

Group	*Average Diameter Cm.*	*Number of Lesions*	*Successful Results Number*	*Successful Results Per cent*
A	under 1	90	90	100 0
B	1 to 2	82	82	100 0
C	2 to 3	24	24	100 0
D	3 or more	21	16	76 2

It is significant that the five unsuccessfully treated cases of basal cell carcinoma of the nose were all classified in group D As a matter of fact, all of these neoplasms were considerably larger than 3 cm. in diameter and it was excessive involvement of tissues beyond the nose itself that forced discontinuance of treatment. Thus in two cases there was excessive involvement of both orbits in two cases there was excessive destruction of the upper lip and maxillary bone while in one case the neoplasm eroded into the brain through the cribiform plate of the ethmoid bone. In these cases treatment could not be carried further without blindness, unwarrented deformity or immediate death.

The effects of previous treatment on prognosis is adverse as indicated by the rate of cure of 95.5 per cent for patients with recurrent lesions as compared to the rate of 99 2 per cent for those who had not received previous treatment. This would be expected mainly because the delay occasioned by the unsuccessful treatment would tend to allow deeper extension of the carcinoma However the fact that 95.5 per cent of recurrent lesions responded to chemosurgical treatment indicates the effectiveness of the method in such cases. By way of contrast, authors using other methods regularly report a much greater drop in the rate of cure in cases of recurrent cancer For example, Magnussen[44] reported a cure rate of 95 1 per cent for previously untreated basal cell carcinoma of the nose but the rate for the cases of recurrent cancer dropped to 69 6 per cent.

The effect of histologic degree of invasiveness on prognosis is appreciable as indicated by the fact that 100 per cent of the sixty patients with carcinoma recorded as having a low degree of invasiveness were cured while only 96 8 per cent of those with highly invasive basal cell carcinomas were cured. However the microscopic control of excision provided by the chemosurgical technic makes it possible to follow out the slender interspersing strands of highly invasive carcinoma as readily as the circumscribed blunt outgrowths of the less invasive carcinoma. The lower rate of cure in the cases with highly invasive neoplasms is more a reflection of the fact that patients with these lesions are more likely to have had unsuccessful treatment with other methods and therefore their neoplasms had time to grow large before they reported for chemosurgical treatment.

The tendency for basal cell carcinoma of the nose to be highly invasive is indicated by the fact that 72 4 per cent of the cases in this series

were so classified Some degree of keratinization was observed in 23.5 per cent of the cancers and melanin pigmentation in 0.9 per cent but neither of these factors appreciably affected the prognosis.

The effect of the site of origin on prognosis is not very great (Table X) The lowest rate of cure was for the root of the nose where deep invasion of the dangerous region of the cribriform plate is an adverse prognostic factor It is noteworthy that all of the lesions which arose in *the nasolabial fold* were cured although carcinomas of this site are generally conceded to be troublesome.

TABLE X
EFFECT OF SITE OF ORIGIN OF BASAL CELL CARCINOMA OF THE NOSE ON FIVE-YEAR END RESULTS

Site	*Number of Lesions*	*Successful Results Number*	*Per cent*
Root	26	25	96 2
Bridge	87	84	96 6
Tip	41	40	97 6
Ala	56	56	100 0
Nasolabial fold	5	5	100 0
Septum	2	2	100 0
All sites	217	212	97 7

Therapeutic Results in Cases of Squamous Cell Carcinoma of the Nose

Altogether fifty nine squamous cell carcinomas of the nose were chemosurgically excised during the twelve years ending six years prior to the date of this writing The cancers ranged from early to far advanced. Previous unsuccessful radiation or surgical treatment had been received by 46.5 per cent of the patients. Regional metastasis was present in five cases.

The fifty-nine consecutive cases were classified in "determinate" and indeterminate" groups (Table XI) The indeterminate group included the cases of 16 patients who died of other causes before the end of the five year period of observation otherwise, no patients were lost from observation before the end of five years The determinate group included forty three cases made up of six unsuccessful results and the thirty-seven successful results.

TABLE XI
FIVE-YEAR END RESULTS FOR SQUAMOUS CELL CARCINOMA OF THE NOSE

This series includes the cases of all patients with histologically proved squamous cell carcinoma, both early and advanced, previously untreated and recurrent, with and without metastasis, who were chemosurgically treated during the twelve year period ending six years prior to this writing

Total number of cases	59
Indeterminate group total number	16
Patients dead from other causes without recurrence	16
Patients lost from observation without recurrence	0
Determinate group total number	43
Unsuccessful results, total number	6
Patients dead, cancer present at death	5
Patients lost from observation with cancer	1
Patients living with cancer	0
Successful results, patients free of cancer for five years or more	37
Five-year rate of cure (37 ÷ 43) × 100	86 4%

Therefore, five year cures were obtained in 86 4 per cent of the forty three determinate cases of squamous cell carcinomas of the nose. As far as could be determined, the primary lesion was eradicated in 91.5 per cent of the cases.

The effect of the size of the lesion on prognosis became appreciable as the average diameter exceeded 3 cm. (Table XII) Thus, five of the six unsuccessful results were in cases in group D Examples of lesions in the various classifications as to size are illustrated as follows group B (diameter 1 to 2 cm.) in Figure 45 group C (diameter 2 to 3 cm.) in Figures 51 56 58 and 64 group D (diameter 3 cm. or more) in Figures 48 54 and 65

TABLE XII
EFFECT OF SIZE OF SQUAMOUS CELL CARCINOMA OF THE NOSE ON FIVE-YEAR END RESULTS

Group	*Average Diameter Cm.*	*Number of Lesions*	*Successful Results Number*	*Per cent*
A	under 1	17	17	100 0
B	1 to 2	14	13	92 9
C	2 to 3	3	3	100 0
D	3 or more	9	4	44 4

The reasons for the impaired prognosis in lesions of large size are the greater chance of metastasis (four cases) and the greater chance

of destruction of such an extent that complete removal was not justified (two cases) Large size in itself is no deterrent to chemosurgical treatment and many very extensive lesions were successfully treated

The effect of previous treatment on prognosis is appreciably adverse as indicated the rate of cure of 75 per cent in the group of patients who received previous radiation or surgical treatment as compared to 95 7 per cent in the group of patients who received no previous treatment.

The delay occasioned by the use of treatments which proved ineffective had an adverse effect because it allowed the neoplasms to become more deep-seated and it increased the chance of metastasis. Moreover previous treatment occasionally had some tendency to produce isolated islands of neoplasm with intervening areas of normal tissue. This lack of continuity gave rise to the danger that although the main mass of cancer might be eradicated an outlying isolated focus might not be located in the sections and would not become apparent until of sufficient size to become clinically visible or palpable. Cold knife surgical excision also can produce outlying foci by dissemination of cells during procedures such as undermining and closure.

The effect of the histologic grade of malignancy on prognosis is considerable. Thus the rate of cure was 100 per cent in grade 1 and 93.3 per cent in grade 2 but it was only 76.9 and 33.3 per cent in grades 3 and 4 respectively (Table XIII) Most of the unsuccessfully treated lesions were extremely invasive and the carcinomatous infiltration proved to be much more deep than had been anticipated on the basis of the initial clinical examination This and the greater incidence of metastasis accounted for the poorer results in the patients with more highly malignant carcinomas. Nevertheless patients with the dangerous highly malignant squamous cell carcinomas often are those in most desperate need of the microscopically controlled excision provided by the chemosurgical technic

TABLE XIII
EFFECT OF HISTOLOGIC GRADE OF MALIGNANCY OF SQUAMOUS CELL CARCINOMA OF THE NOSE ON FIVE-YEAR END RESULTS

Grade	Number of Lesions	Successful Results Number	Successful Results Per cent
1	12	12	100 0
2	15	14	93 3
3	13	10	76 9
4	3	1	33 3

The effect of site of origin on prognosis may be summed up by the generalization that the more posterior the site of origin on the nose the greater the chance of deeply destructive invasion and entrance into larger lymphatic channels. Thus, the rate of cure was less in cases in which the carcinoma arose on the nasolabial fold the septum or the root than it was when the neoplasm arose on the tip bridge or ala (Table XIV)

TABLE XIV
EFFECT OF SITE OF ORIGIN OF SQUAMOUS CELL CARCINOMA OF THE NOSE ON FIVE-YEAR END RESULTS

Site	Number of Lesions	Successful Results Number	Successful Results Per cent
Root	6	5	83 3
Bridge	14	13	92 9
Tip	5	4	80 0
Ala	10	9	90 0
Nasolabial fold	2	1	50 0
Septum	5	4	80 0
Vestibule	1	1	100 0
All sites	43	37	86 4

Examination of the six unsuccessfully treated cases of squamous cell carcinoma of the nose revealed some degree of connection between the site of origin and the cause of failure. Thus in a case in which the lesion began on the root of the nose the cause of failure was invasion of the brain through the cribriform plate of the ethmoid bone. In the other cases in which the cancers were not cured the failures were because of such deep extension into the adjacent facial structures such as the orbits, the maxillary bone the upper lip and the cheeks that it was decided that the radical destruction necessary for their cure was not justified

The effect of metastasis on prognosis in cases of squamous cell carcinoma of the nose would seem to be considerable on superficial examination of the statistics. In the group of five patients with metastasis only one was cured

(20 per cent) while in the group of thirty-eight patients who did not have metastasis there were *thirty six successful results (94 7 per cent)* However metastasis was not the chief cause of failure in the five unsuccessfully treated cases the primary lesion had proven to be too extensive for complete eradication to be feasible and the metastases only added to the hopelessness of the situation.

Comparison of Results with Those of Other Authors

As is the case with cancer of other areas of the skin, the best comparable series of carcinoma of the nose, both as regards the excellence of the results and also the adequacy of statistical evaluation, is that of the Radiumhemmett of Stockholm as reported by Magnussen.[44] In his series of 84 determinate cases of basal cell carcinoma of the nose, the rate of cure at five years was 88 1 per cent as compared to the rate of 97 7 per cent in the present series of 217 determinate cases. The two series were approximately comparable as regards the proportion of large lesions (26.2 per cent of Magnussen s cases were in groups C and D as compared to 21 1 per cent in this series) but his series included fewer cases in which there had been previous unsuccessful treatment (27 4 per cent as compared to 41 per cent in the present series)

In Magnussen s series of seventeen determinate cases of squamous cell carcinoma of the nose the five year rate of cure was 88.2 per cent as compared to the rate of 86.4 per cent in the present series of 43 determinate cases. The two series were essentially comparable as regards the proportion of large lesions (29 4 per cent of Magnussen s cases were in group C and D as compared to 27.9 per cent in the present series) but considerably fewer of his patients had received previous unsuccessful treatment (17 6 per cent as compared to 46.5 per cent in the present series) and his series included no cancers in the more dangerous septal and nasolabial fold areas.

The microscopic guidance of excision afforded by the chemosurgical method not only has provided a reliable means of following out the unpredictable ramifications of cancer into the various parts of the nose but it has made it possible to do this without destroying uninvaded tissue Moreover this was accomplished in this series of 367 cases of carcinoma of the nose without a single death attributable to chemosurgical treatment.

CHAPTER 5

Carcinoma of the Ear

THE conservative excision which may be carried out safely with the chemosurgical method is particularly advantageous in the treatment of cancer of the external ear because extensive defects of this structure are not easy to repair satisfactorily.[87] The microscopic control of excision allows such conservative removal of small lesions that no repair is needed while in the treatment of large lesions a maximum amount of normal tissues is preserved as a basis for reconstruction. Moreover, the healing qualities of the cartilage and other tissues are not impaired by chemosurgical treatment therefore, there is no chance of chronic perichondritis or ulceration such as may follow radiation therapy

The chemosurgical treatment of cancers of each of the various regions of the external ear presents different problems. Accordingly the subject is presented under the following headings (1) helix and lobe (2) antihelix and crura (3) concha (4) canal and deeper structures (5) tragus and preauricular region (6) posterior surface and (7) postauricular sulcus. A feature possessed in common by all of these anatomic regions is a cartilaginous framework covered by a thin layer of skin and subcutaneous connective tissue Because of the thinness of this covering most cancers soon come into contact with the cartilage. Therefore except when the neoplasm is relatively superficial the initial surgical excision and curettage often exposes the perichondrium in the center of the lesion. When this is the case subsequent chemosurgical treatment simply consists of the removal of specimens of fixed tissue from the periphery for microscopic study (Figs. 73 and 74) If the cartilage has been penetrated by the cancer the erosion is readily visible to the naked eye. However to determine whether or not there is involvement of the tissues on the other side of the eroded cartilage requires microscopic examination. Cartilage which has been penetrated by the fixative ordinarily must be removed unless the area is so small that the surrounding granulation tissue can cover readily

Helix and Lobe

Because of their prominent position at the edge of the ear the helix and lobe are unusually subject to deformity as a result of carcinomatous invasion unless the lesion is small. Following chemosurgical excision, a repair sometimes is desirable, but in older people it often is preferable simply to smooth out the sharp edges of the niche during treatment so that the defect is made less noticeable (Fig 66) Even in case of extensive destruction of the helix by carcinoma or irradiation it is worthwhile to be conservative in the removal of the abnormal tissues in order to preserve some semblance of an ear (Fig 67)

Extensive lesions of the upper and anterior portions of the helix may cause a loss of support which could allow the ear to hang downward. However if the normal position of the ear is maintained during the healing process by means of adhesive tape or by means of sutures, this position becomes permanent (Fig 68) Cancer of the anterior extremity of the helix may be chemosurgically excised with little defect even if it has spread out over the adjacent concha and other structures (Fig 69)

Carcinoma of the lobe may require partial or complete removal of this structure but since there normally are such wide variations in



A B C

Fig 66. (A) Squamous cell carcinoma, grade 1 malignancy (B) Granulation tissue after chemosurgical excision. A small amount of the helix above and below the neoplasm also was removed to avoid a sharply defined niche. (C) Healed lesion. The contour of the ear was not unsightly There was no recurrence after five years.



A B C

Fig 67 (A) Mixed basal and squamous cell carcinoma with superimposed painful radiation perichondritis and ulceration. Courses of roentgen therapy had been received ten years and six years previously and there had been persistent ulceration for four years. (B) Granulation tissue after chemosurgical excision. (C) Healed lesion. There was no recurrence after six years.

the contours of the lobe the defect usually is not noticeable (Fig 70)

If after chemosurgical excision of cancers of either the lobe or the helix there is formed an unpleasant outline it is often possible to improve the contour by the removal of tags and eminences. This usually is done during or just after chemosurgical treatment. However if a repair is contemplated, it usually is preferable to preserve all of the uninvolved tissue as a basis for the reconstruction.

In the chemosurgical treatment of cancer of

the helix it is important to remember that cartilage is an avascular tissue through which the fixative penetrates very readily Therefore, care must be exercised to avoid overdosage eral it is preferable to proceed slowly removing thin rather than thick layers of fixed tissue, so that only minimal amounts of normal tissue are destroyed during the removal of the cancer



Fig 68. (A) Basal cell carcinoma. (B) Lesion at completion of chemosurgical treatment with fixed tissue still adherent. The cancer had invaded deeply into the pericranial tissues and had extended in the perichondrium into the helix, crura and concha. (C) Healed lesion. The ear was taped against the scalp during healing until this position became permanent. There was no recurrence after four years.



Fig 69 (A) Keratinizing basal cell carcinoma which had recurred after roentgen therapy excision and electrodesiccation. (B) Granulation tissue after chemosurgical excision. The carcinoma extended for 8 mm. in the perichondrium to the concha (C) Healed lesion. There was no recurrence after four and one-half years.

This caution is especially needed when the main mass of the cancer has been removed by surgical excision and curettement prior to the institution of chemosurgical treatment. In gen

Antihelix and Crura

Carcinomas at the antihelix and crura and of the adjacent sulci often are limited in their

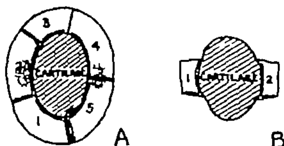


Fig 74 Maps of specimens removed on two successive days from the patient illustrated in Figure 73 (A) Stippled areas represent two areas of cancer (B) The specimens on the next day were free of cancer

complete amputation is necessary the external auditory canal remains widely patent (Fig 75)

and it is feasible to carry out the microscopically controlled excisions as far medially as the middle ear

If the entire circumference of the canal is involved there may be some tendency for stenosis to develop This may be reduced by applying scarlet red gauze or vaseline gauze to the granulating surface and then packing with cotton to produce firm pressure. Exuberant granulation tissue should be cauterized with a silver nitrate stick. The conservatism made possible by the microscopic control of excision *often results in the preservation of part of the* lining of the canal and then the tendency toward stenosis is less. If the stenosis causes the



Fig 75 (A) Squamous cell carcinoma, grade 4 (B) Granulation tissue and exposed mastoid bone after chemosurgical excision. The carcinoma invaded the parotid gland anteriorly and there was an extension along the sheath of a nerve inferiorly (C) Healed lesion. The scar was linear and the canal was patent. There was no recurrence of the primary lesion after two years but when a cervical metastasis developed the patient, who suffered from senile dementia, failed to return until the mass was inoperable.

Canal and Deeper Structures

Neoplasms seldom arise in the external auditory canal. This is fortunate because cancers in this region often tend to spread inwardly to invade the middle ear and other relatively inaccessible structures. However there is no reason why early lesions should not be amenable to cure by chemosurgical treatment. Long *slender knives and forceps are employed to re*move the specimens from the wall of the canal

collection of secretions in the inner portion of the canal and infection ensues, it may prove necessary to reopen the canal. Occasionally a plastic repair is needed to prevent recurrence of the stenosis.

Tragus and Preauricular Region

Carcinomas of the tragus and preauricular region present no problems unless deep invasion into the subjacent tissues has occurred. Thus, extensive involvement of the external auditory

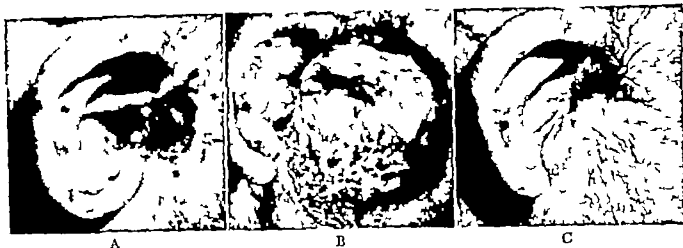


Fig 76. (A) Basal cell carcinoma which had recurred after treatment with radium, roentgen rays and electrodesiccation. For two years the cancer had been invading the ear canal (B) Granulation tissue and exposed capsule of the temporomandibular joint after chemosurgical excision. The entire circumference of the canal was invaded. (C) Healed lesion. The canal almost closed because of exuberant granulation tissue formed in response to necrotic bone which was not thrown off promptly because of the previous radiation therapy After reopening the canal remained widely patent (C) Healed lesion. There was no recurrence when the patient died of other causes after nine years.



Fig 77 (A) Squamous cell carcinoma, grade 2 (B) Granulation tissue after chemosurgical excision. (C) Healed lesion. There was no recurrence after five years.

canal may cause some tendency toward stenosis but this may be minimized by packing the canal as has been described Sometimes the temporomandibular joint is invaded but this complication is not serious as ankylosis never develops (Fig 76) Finally the external carotid or superficial temporal arteries may be approached with consequent danger of hemorrhage This complication may be prevented by inserting a suture ligature if pulsation observed during excision suggests that the vessel is being too closely approached Deeply invasive lesions may also necessitate the interruption of part or all of the primary branches of the facial nerve.

Posterior Surface

Carcinomas on the posterior surface of the auricle *often* are found to have invaded to the cartilage This usually means that some cartilage

must be removed before healing can proceed to completion. Wounds of moderate size usually heal with barely visible scars and no defect (Fig 77)

Postauricular Sulcus

Cancers arising in the sulcus formed by the junction of the ear and postauricular scalp often are found to extend rather deeply into the functional tissues. However even lesions of fairly wide extent heal with fine linear scars (Fig 78) Deep lesions may erode to the cranium but this is not a dangerous complication unless the bone is penetrated. Then entrance into the venous sinuses and into the meninges may be hazards.



Fig 78. (A) Basal cell carcinoma which had recurred after treatment with a caustic chemical. (B) Granulation tissue after chemosurgical excision. (C) Healed lesion. There was no recurrence after six years.

Therapeutic Results in Cases of Basal Cell Carcinoma of the Ear

Altogether seventy four basal cell carcinomas of the ear were chemosurgically excised during the twelve year period ending six years prior to the date of this writing The cancers were in all stages from early to advanced. Thirty-one per cent of the patients had received previous unsuccessful treatment. There were no metastases.

The seventy four consecutive cases were divided into "indeterminate" and "determinate" groups. The indeterminate group included the cases of nineteen patients who died of intercurrent disease before the expiration of the five year period without evidence of recurrence and the three patients who were lost from observation before the end of five years but who were without evidence of cancer when last seen. The determinate group included the cases of three patients who were unsuccessfully treated and the cases of forty nine patients who were successfully treated (Table XV)

Thus, after observation for five years or more, successful results were obtained in forty nine of the fifty-two determinate cases. Therefore, the rate of cure at five years was 94.2 per cent.

The effect of the size of the lesion on prognosis was slight unless the average diameter of the basal cell carcinoma exceeded 2 cm. because all of the neoplasms smaller than this size were cured. However the cure rate dropped in group C (diameter 2 to 3 cm.) and group D (diameter, 3 cm. or more) to 90 per cent and 75 per cent respectively (Table XVI) Examples of basal cell carcinomas of various sizes are illustrated as follows group B (diameter 1 to 2 cm.) in Figure 69 group C (diameter 2 to 3 cm.) in Figures 68, 70, 76 and 78 and group D (diameter 3 cm. or more) in Figure 67

TABLE XV

FIVE-YEAR END RESULTS FOR BASAL CELL CARCINOMA OF THE EAR

This series includes the cases of all patients with histologically proved basal cell carcinoma, both early and advanced previously untreated and recurrent, who were chemosurgically treated during the twelve year period ending six years prior to this writing

Total number of cases	74
Indeterminate group, total number	22
Patients dead from other causes without recurrence	19
Patients lost from observation without recurrence	3
Determinate group total number	52
Unsuccessful results, total number	3
Patients dead, cancer present at death	3
Patients lost from observation with cancer	0
Patients living with cancer	0
Successful results, patients free of cancer for five years or more	49
Five-year rate of cure (49 ÷ 52) × 100	94 2%

The three unsuccessfully treated patients had large cancers but it was not the size *per se* that accounted for the poor results. Rather it was the deep invasion of underlying structures that caused the failures. Thus the canal and middle ear were involved in one case while in two other cases the dura and deep cervical tissues were involved.

TABLE XVI

EFFECT OF SIZE OF BASAL CELL CARCINOMA OF THE EAR ON FIVE-YEAR END RESULTS

Group	Average Diameter Cm	Number of Lesions	Successful Results Number	Per cent
A	under 1	16	16	100
B	1 to 2	17	17	100
C	2 to 3	10	9	90
D	3 or more	9	7	75

The effect of previous treatment on prognosis is somewhat adverse as indicated by the fact that the rate of cure in the group of patients who had received previous treatment was only 87.5 per cent as compared to 97.2 per cent for the group who had not received previous treatment. However one of the prime uses for chemosurgical treatment is in the case of the patient whose cancer has proved refractory to other types of treatment and the fact that 87.5 per cent of the patients with recurrent cancers were cured indicates the effectiveness of this method in such cases The chief reason for the adverse influence of recurrence on prognosis is the delay occasioned by the prolonged use of ineffectual treatment. Thus in two of the unsuccessfully treated patients of this series the carcinomas had had time to invade through the cranium to the dura and in one the carotid artery in the upper cervical region was involved Sometimes the radiation or surgical treatment keeps the superficial portion of the neoplasm under apparent control but allows the deep portion to continue its growth unsuspected for a considerable time. Moreover these treatments may eradicate parts of the neoplasm and leave several isolated foci In the case of cold knife excision, there also is the possibility of the implantation of cancer cells in the surrounding tissues. However it is produced, this discontinuous type of spread may be the cause of incomplete removal in spite of the microscopic control afforded by the chemosurgical technic.

The effect of the histologic degree of invasiveness on prognosis is definitely adverse as indicated by the fact that the rate of cure for the group of patients with highly invasive basal cell carcinomas of the ear was only 92.5 per cent as compared to 100 per cent for the group with carcinomas of a low degree of invasiveness. However this does not signify that the chemosurgical method is less effective in the treatment of highly invasive lesions. On the contrary the microscopic control of excision makes it possible to follow out the interspersing strands of highly invasive carcinoma just as reliably as the globular protrusions of the less invasive carcinoma What the lower rate of cure associated with highly invasive lesions does signify is that these cancers are more likely to have been recurrent after other treatment and to have spread to the deep structures such as the dura and the middle ear

There was keratinization of some degree in 13.5 per cent of the basal cell carcinomas but this feature exerted no appreciable effect on prognosis. Most of the keratinization was in the more highly invasive carcinomas, particularly in those which had recurred after irradiation. None of the basal cell carcinomas of the ear contained melanin pigment

The effect of the site of origin on the prognosis of basal cell carcinoma of the ear consists of an adverse influence of medial position. Thus, the three unsuccessfully treated patients had cancers arising in the concha, canal and postauricular sulcus respectively Apparently, the nearer the neoplasms are to inaccessible and vital structures, the greater the likelihood of their invasion. By contrast the neoplasms which arose on the protruding portion of the ear were cured in all cases (Table XVII)

TABLE XVII
EFFECT OF SITE OF ORIGIN OF BASAL CELL CARCINOMA OF THE EAR ON FIVE-YEAR END RESULTS

Site	*Number of Lesions*	*Successful Results Number*	*Per cent*
Helix	7	7	100 0
Lobe	2	2	100 0
Antihelix and crura	3	3	100 0
Concha	6	5	83 3
Canal and deeper structures	1	0	0
Tragus and preauricular	10	10	100 0
Posterior surface	12	12	100 0
Postauricular sulcus	11	10	90 9
All sites	52	49	94 2

Therapeutic Results in Cases of Squamous Cell Carcinoma of the Ear

In all, seventy six squamous cell carcinomas of the ear were excised during the twelve year period ending six years prior to the date of this writing The cancers were in all stages from early to advanced. Previous unsuccessful treatment had been received by 35 2 per cent of the patients. There was metastasis in the regional nodes in eight cases (14.8 per cent of the determinate cases)

The seventy-six consecutive cases were divided into "indeterminate" and determinate" groups. The indeterminate group included the cases of twenty two patients who died of intercurrent disease before the elapse of five years without evidence of recurrence. The determinate group included the cases of eleven patients who were unsuccessfully treated and the cases of forty three patients who were successfully treated (Table XVIII)

Thus after observation for five years or longer successful results were obtained in forty three of the fifty four determinate cases. Therefore, the rate of cure at five years was 79.6 per cent. As far as could be determined the primary lesion was eradicated in 92.1 per cent of the cases.

TABLE XVIII
FIVE YEAR END RESULTS FOR SQUAMOUS CELL CARCINOMA OF THE EAR

This series includes the cases of all patients with histologically proved squamous cell carcinoma, both early and advanced, previously untreated and recurrent, with and without metastasis, who were chemosurgically treated during the twelve year period ending six years prior to this writing

Total number of cases	76
Indeterminate group total number	22
Patients dead from other causes without recurrence	22
Patients lost from observation without recurrence	0
Determinate group, total number	54
Unsuccessful results, total number	11
Patients dead, cancer present at death	11
Patients lost from observation with cancer	0
Patients living with cancer	0
Successful results, patients free of cancer for five years or more	43
Five-year rate of cure (43 ÷ 54) × 100	79 6%

The effect of the size of the lesion on prognosis is definite as indicated by the drop in the rate of cure from 100 per cent in the group with lesions under one centimeter in diameter to 50 per cent in the group with lesions three centimeters or more in diameter (Table XIX)

TABLE XIX
EFFECT OF SIZE OF SQUAMOUS CELL CARCINOMA OF THE EAR ON FIVE-YEAR END RESULTS

Group	*Average Diameter Cm.*	*Number of Lesions*	*Successful Results Number*	*Per cent*
A	under 1	18	18	100 0
B	1 to 2	17	15	88 2
C	2 to 3	7	4	57 1
D	3 or more	12	6	50 0

Examples of squamous cell carcinomas of various sizes are illustrated as follows group B (diameter 1 to 2 cm.) in Figures 71 and 73 group C (diameter 2 to 3 cm.) in Figures 66 72 and 77 and group D (diameter 3 cm. or more) in Figure 75

The reasons for unsuccessful results being more common in the cases with large lesions

are the greater likelihood of involvement of vital structures and the greater incidence of metastasis. Thus, in this series all of the unsuccessfully treated patients either had metastasis (eight cases) or invasion of such deep structures as the middle ear, the pharynx, or the meninges and the transverse venous sinus (three cases) These complications, rather than large size per se, were the direct causes of failure. Nonetheless, large size and poor prognosis did go together as indicated by the fact that in the unsuccessfully treated cases the size of the cancers, as measured prior to the institution of treatment, placed two cases in group B three cases in group C, and six cases in group D

The effect of previous treatment on prognosis is appreciable as indicated by the rate of cure of 57.9 per cent in the nineteen cases with previously treated lesions as compared to 91 4 per cent in the thirty five cases with untreated lesions. This drop in the rate of cure in the cases in which the patients had received previous treatment is to be expected, largely because of the delay which allowed the cancers to spread to inaccessible structures and to metastasize. However the fact that over half of the patients whose cancers did not yield to other treatments were successfully treated by means of chemosurgery indicates the usefulness of this method in the treatment of recurrent squamous cell carcinoma of the ear

The effect of histologic grade of malignancy on prognosis is considerable. This is indicated by the drop in the rate of cure from 90.9 and 92 9 per cent in the cases with cancers of grade 1 and 2 malignancy to 60 and 20 per cent in those with grade 3 and 4 malignancy (Table XX) Most of the adverse effect of high malignancy was due to the greater likelihood of metastasis but to some extent it was also due to the greater likelihood of invasion of deep vital structures Barring these complicating factors the highly malignant cancers were just as readily removed by the chemosurgical technic as the less malignant neoplasms although the unpredicted infiltrating extensions from the main mass were more common in the former

The effect of the site of origin on the prognosis in cases of squamous cell carcinoma of the ear is noteworthy in that the more medial the origin the less the chance of cure. Thus none of the patients with cancers which arose in the canal or in deeper structures were cured while all of those with cancers on the helix, lobe and concha were cured In between these extremes were the patients with cancers which arose on the tragus and preauricular region, on the posterior surface of the ear and in the postauricular sulcus with about 75 per cent cures and those with cancer on the antihelix and crura with over 90 per cent cures (Table XXI)

TABLE XX

EFFECT OF HISTOLOGIC GRADE OF MALIGNANCY OF SQUAMOUS CELL CARCINOMA OF THE EAR ON FIVE-YEAR END RESULTS

Grade	Number of Lesions	Successful Results Number	Per cent
1	11	10	90 9
2	28	26	92 9
3	10	6	60 0
4	5	1	20 0

TABLE XXI

EFFECT OF SITE OF ORIGIN OF SQUAMOUS CELL CARCINOMA OF THE EAR ON FIVE-YEAR END RESULTS

Site	Number of Lesions	Successful Results Number	Per cent
Helix	11	11	100 0
Lobe	1	1	100 0
Antihelix and crura	15	14	93 3
Concha	2	2	100 0
Canal and deeper structures	5	0	0
Tragus and preauricular	4	3	75 0
Posterior surface	9	7	77 8
Postauricular sulcus	7	5	71 4
All sites	54	43	79 6

The poor prognosis associated with carcinomas of the external auditory canal in this series was the result of extensive deep invasion in all five cases and, in addition, metastasis in three cases. In one case the cancer extended along the periosteum over the temporal and parietal bones, into the middle and inner ear and down the eustachian tube. In another case the cancer extended into the postpharyngeal region and involved the jugular vein. Ob-

viously such extensive involvement precludes a successful outcome but there was no way of knowing the exact extent of these neoplasms until the extensions had been followed out with the microscopically controlled chemosurgical excisions. However there is no reason why cancers which have not extended so far beyond the external auditory canal should not be curable.

There were five unsuccessfully treated cancers which arose in or near the attachment of the pinna to the post or preauricular tissues (tragus and preauricular, posterior surface, and postauricular sulcus) It seems likely that these failures were due to three factors (1) nearness to the deeper vital structures (2) nearness to the larger lymphatic vessels, and (3) frequent traumatization of the cancer by movements of the auricle. The last two factors explain the high rate of metastasis in these areas (four of the five unsuccessfully treated patients with cancer in these areas had metastases)

The high rate of cure associated with lesions of the helix, lobe, concha, antihelix and crura is probably in part due to the lack of motion which might squeeze cancer cells out into the lymphatics but is also due to the greater distance between the cancer on the one hand and vital structures and larger lymphatics on the other

The effect of metastasis on the prognosis of squamous cell carcinoma of the ear is very unfavorable. In this series there were eight cases in which there was metastasis and in all of these the outcome was unfavorable. In contrast, there were forty-six patients without metastasis and of these forty-three were successfully treated (93.5 per cent)

In this series only three patients had metastases which were deemed operable. In six cases deep roentgen therapy was given for palliation. No prophylactic neck dissections were carried out.

In spite of the poor results in patients with metastases in this series the prognosis in such cases should not be considered hopeless and close postchemosurgical observation should be carried out with the object of early detection and surgical treatment of regional metastasis.

Comparison of Results with Those of Other Authors

For comparison with effectively used radiologic, surgical and electrosurgical technics the statistically adequate data of Magnussen[45] are useful. From his protocols it was determined that in his series of twenty-one determinate cases of basal cell carcinoma of the ear the five-year cure rate was 76.2 per cent as compared to 94.2 per cent in the present series of fifty two determinate cases. Magnussen's series included a few more cancers of large size (47.4 per cent were 2 cm. or more in diameter as compared to 36.5 per cent in the present series) but not as many cancers were recurrent after previous treatment elsewhere (23.7 per cent as compared to 30.8 per cent in this series)

Magnussen's series included twenty determinate cases of squamous cell carcinoma of the ear and the five-year cure rate was 50 per cent as compared to 79.6 per cent in the present series of fifty four determinate cases. More of his lesions were classified in groups C and D (2 cm. or more in diameter) than in the present series (62.5 per cent as compared to 35.2 per cent) but his series included only four very large lesions (group D) while the present series included twelve cases in this group Approximately the same proportion of patients had been unsuccessfully treated elsewhere in both series (35 per cent as compared to 35.2 per cent)

Therefore, in the two comparable series of cases the five-year cure rate for chemosurgically treated basal cell carcinoma was 94.2 per cent as compared to 76.2 per cent in Magnussen's series, while for squamous cell carcinoma the rate for chemosurgically treated cases was 79.6 per cent as compared to 50 per cent in Magnussen's series.

The microscopic control of excision provided by the chemosurgical technic was responsible not only for the unprecedented reliability but also for the conservatism which allowed the preservation of portions of the ear which otherwise would have been destroyed. In addition, in this series of 150 cases of carcinoma of the ear the operative mortality rate was zero.

CHAPTER 6

Carcinoma of the Eyelids

CARCINOMA of the eyelids may be treated chemosurgically without danger of damage to the eyeball unless the sclera is involved to such an extent that its entire thickness must be penetrated to permit complete removal of the neoplasm.[89] The mechanisms by which the eyeball is protected during chemosurgical treatment are two-fold (1) the lid edema and chemosis tend to push the treated area away from the eyeball, and (2) the tears dilute the fixative chemical as it slowly permeates through the lids with the result that the concentration does not become sufficient to damage the eyeball.

It is obvious that the fixative must be applied in such a manner that it won t be carried into the eye by the tears or by the movements of the eyelids. If a neoplasm near the lid margin is being treated chemosurgically without preliminary surgical excision, the first application is made to the portion of the tumor away from the lid margin. In this way an excavation is made from which further chemosurgical treatment may be carried out safely Usually however the excavation is produced by preliminary surgical excision and curettage which are done under local anesthesia. This surgical procedure not only is faster but it is less painful and there is less opportunity for irritation of the eye by the inadvertant entrance of the fixative chemical into the eye

After the excavation is produced the chemosurgical procedure is the same as in other locations except that extra care is exercised in the application of the dressing in order to prevent shifting by the movements of the eyelids or wetting by the tears. The dressings are made small and are fitted as accurately as possible so that they may be securely taped in place, if too large, the dressings can move slightly under the adhesive tapes. If the lesion is in an area where the dressing is likely to be soaked with tears extra precautions are required to make the dressing occlusive. Often this is accomplished by the use of a double layer of petrolatum gauze applied over the thin layer of cotton which covers the fixative. When properly done this keeps the tears away from the applied fixative even though the overlying dressing may become wet. Often the eye is kept closed with an eyepatch to prevent unnecessary tearing and blepharospasm this in turn helps to prevent wetting and movement of the dressing

If the cancer is so extensive that the eye must be removed this may be accomplished either by continuing with the chemosurgical technic or by surgical removal. If the eye is to be removed chemosurgically the conjunctiva is anesthetized with 4 per cent cocaine solution, and the surrounding tissues including the ciliary ganglion are infiltrated with procaine Then the sensitive conjunctival and scleral tissues are rapidly destroyed with dichloracetic acid and zinc chloride fixative This rapidly eliminates tearing and the eye may be removed in the same manner as any other tissue.

Carcinoma of the eyelid may be considered according to the site of origin under four headings as follows lower eyelid upper eyelid, medial canthus and lateral canthus

Lower Eyelid

Cancers of moderate size located several millimeters from the lid margin may be chemosurgically excised without concern about the lid being pulled downward because there is enough elasticity in the eyelid tissues to com

pensate for the scar contraction (Fig 79) However if the cancer is at or near the lid margin, ectropion will develop unless the lid margin, including a small amount of the conjunctiva, also is removed. When the cancer involves the edge of the lid the tissues at the lid margin necessarily are removed and no ectropion results (Fig 80) However if the cancer spares a thin strip of the lid margin it is necessary to sacrifice this marginal tissue to avoid its eversion as the scar contracts (Fig 81)

It is remarkable how the lower lid will pull into normal position after the removal of a considerable amount of tissue. The functional and cosmetic results usually are nearly perfect except for the lack of the lashes which are unimportant on the lower lid. Even eyelids which have been pulled down by the weight of the



Fig 79 (A) Basal cell carcinoma which had recurred after electrodesiccation. (B) Granulation tissue after chemosurgical excision. (C) Healed lesion. There was no recurrence when the patient died of other causes after three and one-half years.

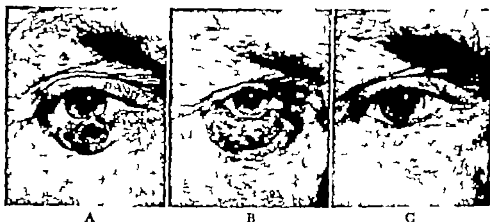


Fig 80 (A) Basal cell carcinoma which had recurred after treatment with caustics and electrodesiccation. (B) Granulation tissue after chemosurgical excision. The neoplasm invaded the palpebral conjunctiva and this necessitated removal of the lid margin and a narrow strip of conjunctiva. (C) Healed lesion. The lid has pulled up into normal position. There was no recurrence after four years.

A B C

D

Fig 81 (A) Basal cell carcinoma which had recurred after electrodesiccation treatment. (B) Lesion during chemosurgical treatment. The lines on the fixed tissue indicate the origin of the five specimens which had been removed for frozen sections. Microscopic examination revealed cancer in the central portion, but this area was free of cancer when the next layer was excised. Though the lid margin was free of cancer a narrow strip of conjunctiva was sacrified to avoid ectropion. (C) Granulation tissue after separation of the final layer of fixed tissue (D) Healed lesion. This is the normal position of the eyelid for this patient. There was no recurrence after five years.



Fig. 82. (A) Squamous cell carcinoma, grade 1 malignancy The weight of the tumor had caused eversion with resultant conjunctivitis. (B) Granulation tissue after chemosurgical excision. (C) Healed lesion. The contraction of the scar has pulled the lid up into normal position. There was no recurrence when the patient died of other causes after two years.

cancer will return to normal position upon removal of the neoplasm and the adjacent lid margin (Fig 82) The cosmetic results are so good that even if the lid margin were saved and a graft placed to prevent eversion, it is doubtful if the appearance would be any better

Cancers which predominantly involve the conjunctival side of the lower lid may require the sacrifice of some uninvolved tissue on the cutaneous side of the lid but the return to normal position is so rapid and complete that the loss is of little consequence (Fig 83)

More advanced cancers may extend posteriorly for some distance into the orbit. Fortunately there is a strong tendency for most of these neoplasms to remain close to the wall of the orbit and to spare the eye (Fig 84)

The entire *lower* eyelid has been removed in a number of cases. There is no danger of damage to the eye from exposure because the upper lid extends far enough down to provide adequate closure (Fig 85) Patients with carcinomatous invasion of the bulbar conjunctiva have also been treated by means of chemosurgical excisions carried out at intervals of minutes instead of hours. In such cases atropine is instilled in the eye or administered parenterally to reduce tearing and great care is used to avoid more than superficial damage to the sclera. If the extension of the cancer into the orbit is extensive or if the eyeball itself is involved the eye must be removed (Fig 86)



Fig 83 (A) Basal cell carcinoma with most of the involvement on the conjunctival side. (B) Granulation tissue after chemosurgical excision. The initial treatment consisted of the excavation of the inferior portion of the tumor producing a cavity from which to carry on subsequent chemosurgical excisions. (C) Healed lesion after three weeks. The contour of the eyelid had returned to normal There was no recurrence after five years.

Upper Eyelid and Eyebrow

Because of the elasticity of the skin of the upper eyelid, neoplasms of considerable size may be chemosurgically excised without appreciable defect (Fig 87) Even if the full thickness of the eyelid has been invaded by the carcinoma, the resultant hole through the eyelid, if of moderate size, tends to close spontaneously (Fig 88) In cases in which the lesion directly overlies the cornea, this membrane is not damaged because the tears carry away the chemical as fast as it permeates through the lid (Fig. 89)

Of course there is a limit to the amount of upper eyelid which can be removed without jeopardizing the eyeball through exposure. However in some cases the entire upper eyelid has been removed. This is accomplished without damage to the eye by taping the lower eyelid up over the eyeball and using ophthalmic ointment to prevent exposure until the lower lid can be sutured to the stump of the upper eyelid. Later on, the lower eyelid may be split to provide both upper and lower lids.

Carcinomas in the eyebrow region may be chemosurgically excised with such conservatism that the appearance often is little altered (Fig 90)

Medial Canthus

Following the chemosurgical removal of inner canthal neoplasms the functional and

cosmetic results are surprisingly good even if the carcinoma has been extensive (Fig 91) With lesions of moderate size the resultant scar often is visible only on close inspection and the some separation of the medial portions of the upper and lower lids. Whenever the commissural tissues have been removed to such an extent that the eyelids pull apart, a medial



Fig 84 (A) Basal cell carcinoma which had recurred after three courses of radium treatment and surgical excision. These procedures had kept the superficial portion of the lesion under control but the deep extensions grew unchecked (B) Granulation tissue after chemosurgical excision. The carcinoma invaded for two centimeters posteriorly in the periosteum of the floor and medial wall of the orbit as well as in that of the nasal bone and the lacrimal fossa. The irregular outlines of the neoplasm are evident in the reconstruction of the cancer shown in the insert. (C) Healed lesion. Binocular vision was preserved. (D) Lesion after repair by Dr A B. Hyslop There was no recurrence after fifteen years.

defect is nil (Fig 92) The contraction of the scar tends to pull the commissure together unless there is extensive involvement above and below the canthus in which case there may be tarsorrhaphy should be done in the region of the separation. If the remaining eyelid tissues tend to pull laterally with exposure of the medial portion of the conjunctiva the medial



A B C

Fig 85 (A) Basal cell carcinoma which had recurred after treatment with roentgen rays. (B) Granulation tissue after chemosurgical excision. All except the lateral end of the lower lid was invaded as was the medial canthal region. (C) Healed lesion. The ectropion could have been prevented by the removal of the small fragment of the lateral end of the lower lid. There was no recurrence when the patient died of other causes after six years.

A B C

D

Fig 86. (A) Basal cell carcinoma which had been kept under control superficially for fifteen years by fourteen radium treatments. (B) Granulation tissue after chemosurgical excision. The cancer involved the entire antrum, the periosteum of the nasal bone and so much of the floor of the orbit that the eye had to be removed. (C) Healed lesion showing antrum lined with mucosa. There was no recurrence after fifteen years. (D) Reconstruction of the cancer showing the clinically visible portion (central dark area) and the palpable portion (light area) as contrasted with the actual, microscopically proved extent (whole model)

d of the lids should also be sutured to the lera or other suitable tissue in the inner can- al region. The sutures may be removed when e position of the tissues has become stabilized d no further abnormal exposure is antici ted. Deep invasion may necessitate the de- uction of the lacrimal sac and this may result in some tearing upon exposure to the wind. Slight eversion of the medial part of the lids may take the lacrimal puncta away from its normal position against the eyeball and this also may cause some tearing on exposure. However this symptom has caused little or no incon- venience to most patients.

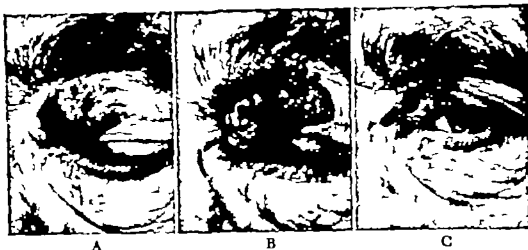


Fig 87 (A) Basal cell carcinoma. (B) Granulation tissue after chemosurgical excision. (C) Healed lesion. There was no recurrence after six years.

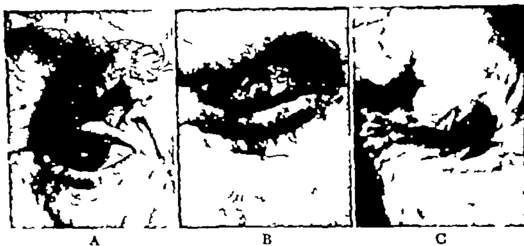


Fig 88 (A) Squamous cell carcinoma, grade 2 malignancy (B) Granulation tissue and hole through the entire thickness of the lid. The iris and pupil are visible through the hole which was necessarily produced because of carcinomatous invasion of the conjunctiva. (C) Healed lesion. The hole closed spontaneously within one month. There was no recurrence when the patient died of other causes after five years.

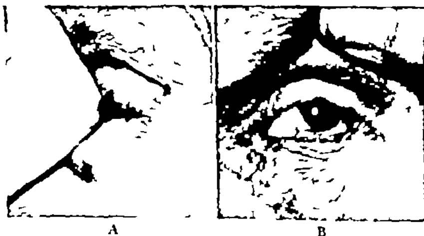


Fig 89 (A) Basal cell carcinoma which extended through the full thickness of the lid directly over the cornea. (B) Healed lesion. There was no damage to the eye because the fixative chemical was diluted by the tears as it slowly permeated through the eyelid.



Fig 85 (A) Basal cell carcinoma which had recurred after treatment with roentgen rays. (B) Granulation tissue after chemosurgical excision. All except the lateral end of the lower lid was invaded as was the medial canthal region. (C) Healed lesion. The ectropion could have been prevented by the removal of the small fragment of the lateral end of the lower lid. There was no recurrence when the patient died of other causes after six years.

A B C

D

Fig 86 (A) Basal cell carcinoma which had been kept under control superficially for fifteen years by fourteen radium treatments. (B) Granulation tissue after chemosurgical excision. The cancer involved the entire antrum, the periosteum of the nasal bone and so much of the floor of the orbit that the eye had to be removed. (C) Healed lesion showing antrum lined with mucosa. There was no recurrence after fifteen years. (D) Reconstruction of the cancer showing the clinically visible portion (central dark area) and the palpable portion (light area) as contrasted with the actual, microscopically proved extent (whole model)

end of the lids should also be sutured to the sclera or other suitable tissue in the inner canthal region. The sutures may be removed when the position of the tissues has become stabilized and no further abnormal exposure is anticipated. Deep invasion may necessitate the destruction of the lacrimal sac and this may result in some tearing upon exposure to the wind. Slight eversion of the medial part of the lids may take the lacrimal puncta away from its normal position against the eyeball and this also may cause some tearing on exposure. However this symptom has caused little or no inconvenience to most patients.



Fig 87 (A) Basal cell carcinoma. (B) Granulation tissue after chemosurgical excision. (C) Healed lesion. There was no recurrence after six years.



Fig 88 (A) Squamous cell carcinoma, grade 2 malignancy (B) Granulation tissue and hole through the entire thickness of the lid. The iris and pupil are visible through the hole which was necessarily produced because of carcinomatous invasion of the conjunctiva. (C) Healed lesion. The hole closed spontaneously within one month. There was no recurrence when the patient died of other causes after five years

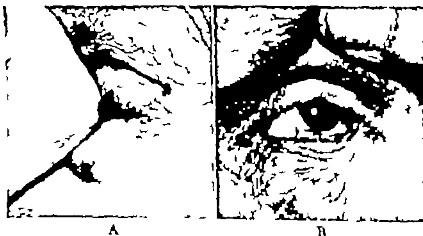


Fig. 89 (A) Basal cell carcinoma which extended through the full thickness of the lid directly over the cornea (B) Healed lesion. There was no damage to the eye because the fixative chemical was diluted by the tears as it slowly permeated through the eyelid.

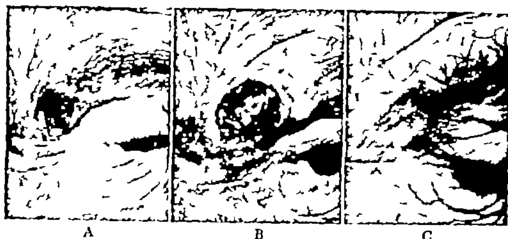


Fig 90 (A) Basal cell carcinoma. (B) Granulation tissue after chemosurgical excision. (C) Healed lesion. There was no recurrence after five years.

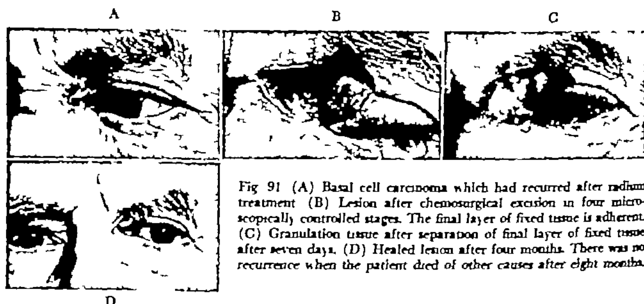


Fig 91 (A) Basal cell carcinoma which had recurred after radium treatment (B) Lesion after chemosurgical excision in four microscopically controlled stages. The final layer of fixed tissue is adherent. (C) Granulation tissue after separation of final layer of fixed tissue after seven days. (D) Healed lesion after four months. There was no recurrence when the patient died of other causes after eight months.



Fig. 92. (A) Basal cell carcinoma. (B) Granulation tissue after chemosurgical excision. An extension into the upper eyelid had not been recognized by clinical examination. (C) Healed lesion. There was no recurrence after five years.

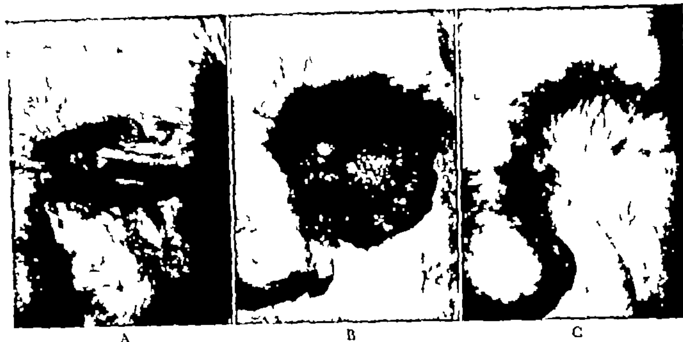


Fig 93 (A) Basal cell carcinoma which started in the medial canthal region and extended over a period of twenty years to involve all of the upper and lower lids and also the orbit including the eyeball. (B) Granulation tissue after chemosurgical excision of the lids, the eye and other orbital contents. A layer of involved bone around the rim of the orbit also was removed as were extensions into the ethmoid sinuses and nasal cavity (C) Healed lesion There was no recurrence after ten years.



Fig 94 (A) Squamous cell carcinoma, grade 3 malignancy The cancer had recurred after electrosurgical removal and twenty four roentgen ray treatments. (B) Granulation tissue after chemosurgical excision. There was extensive invasion of the sclera in the region of the attachment of the medial rectus muscle and therefore the eye was chemosurgically removed. There also was considerable invasion of the nasal mucosa and the ethmoid and maxillary sinuses. (C) Healed lesion before the repair There was no recurrence after eight years.

Neglected cancers (Fig 93) or highly malignant cancers which had proved refractory to other methods of treatment (Fig 94) often still are curable by chemosurgical treatment. The only limiting factor is carcinomatous invasion of the brain through the inferior orbital fissure or through the thin bone of the superior wall of the orbit.

Lateral Canthus

Carcinomas of the outer canthal region may be removed without complications if not too

extensive (Fig. 95) However since there is not much room between the outer rim of the orbit and the eyeball, advanced recurrent cancer not infrequently invades the sclera to such an extent that the removal of the eye is necessary (Fig 96) In cases in which carcinomatous invasion necessitates the removal of the lacrimal gland, the other glands of the lids supply sufficient lubrication for the eye. Excessive destruction of lateral canthal tissues may necessitate a lateral tarsorrhaphy to prevent separation of the lids and exposure of the eye.



Fig 95 (A) Basal cell carcinoma. (B) Granulation tissue after chemosurgical excision. (C) Healed lesion. There was no recurrence after three years.



Fig 96. (A) Basal cell carcinoma which had recurred after many treatments with roentgen rays which had caused corneal opacity (B) Granulation tissue after chemosurgical excision. The periosteum of the lateral rim of the orbit and of the adjacent frontal bone was invaded as was the sclera of the eyeball which was chemosurgically removed. (C) Healed lesion. There was no recurrence when the patient died of other causes after two years.

Therapeutic Results in Cases of Basal Cell Carcinoma of the Eyelids

In all, 129 basal cell carcinomas were chemosurgically excised during the twelve year period ending six years prior to this writing The cancers were in all stages from early to advanced. One third of the patients had received previous unsuccessful treatment. There were no metastases.

The 129 cases were divided into "indeterminate" and "determinate" groups. The inde-

terminate group was composed of the cases of thirty four patients who died of intercurrent disease before the lapse of five years without recurrence and the cases of four patients who were lost from observation without recurrence when last seen. The determinate group included the cases of six patients who were unsuccessfully treated and the cases of eighty five patients who were successfully treated (Table XXII)

TABLE XXII
FIVE-YEAR END RESULTS FOR BASAL CELL CARCINOMA OF THE EYELIDS

This series includes the cases of all patients with histologically proved basal cell carcinoma, both early and advanced, previously untreated and recurrent who were chemosurgically treated during the twelve year period ending six years prior to this writing

Total number of patients	129
Indeterminate group, total number	38
Patients dead from other causes without recurrence	34
Patients lost from observation without recurrence	4
Determinate group, total number	91
Unsuccessful results, total number	6
Patients dead cancer present at death	3
Patients lost from observation with cancer	3
Patients living with cancer	0
Successful results, patients free of cancer for five years or more	85
Five-year rate of cure (85 + 91) × 100	93 4%

Therefore, after observation for five years or more, successful results were obtained in eighty five of ninety-one determinate cases of basal cell carcinoma of the eyelids. Hence, the rate of cure at five years was 93 4 per cent.

The effect of the size of the lesion on prognosis was slight in the cases in which the cancer was less than three centimeters in diameter because a high proportion of these were successfully treated. It was only when the size exceeded three centimeters that a significant drop in the rate of cure occurred (Table XXIII) Actually when chemosurgical treatment is used the size itself should have virtually no effect on the rate of cure of basal cell carcinoma unless the lesion is so extensive that there has been invasion through the roof of the orbit or through the inferior orbital fissure. However in lesions of large size there is somewhat more chance of missing some of the numerous rami

TABLE XXIII
EFFECT OF SIZE OF BASAL CELL CARCINOMA OF THE EYELIDS ON FIVE-YEAR END RESULTS

Group	Average Diameter Cm.	Number of Lesions	Successful Number
A	under 1	45	44
B	1 to 2	33	32
C	2 to 3	5	5
D	3 or more	8	4

fications and this is what happened in extremely advanced carcinomas which treated early in this series There wer patients with unsuccessfully treated canc smaller size and both of these failures we to the patient s refusal of enucleation w became apparent that the eyeball had invaded one of these patients received ro therapy elsewhere and the other finally h recommended enucleation in another cit amples of basal cell carcinomas of variou are illustrated as follows group A, (dia under 1 cm.) in Figure 89 group B (dia 1 to 2 cm.) in Figures 79 80 81 83 and 92 group C (diameter 2 to 3 cm Figures 87 and 95 and group D (dia over 3 cm.) in Figures 84 85 86 93 and 9

The effect of previous treatment on the *nosis* in patients with basal cell carcino the eyelids is appreciable as indicated l cure rate of 83.3 per cent in the thirty p who had received previous treatment as pared to the rate of 98 4 per cent in the one patients who had received *no prior* ment. However the microscopically con excisions which characterize the chemos method make possible the salvage of advanced recurrent lesions and *often* th be done without the loss of the eye.

The effect of histologic degree of invas on the prognosis of basal cell carcinoma eyelid is *considerable*. This is indicated l five year rate of cure of 87.8 per cent forty nine cases of carcinoma of a high of invasiveness as compared to the rate per cent in the *forty-two* cases with a lo gree of invasiveness. The lower rate o associated with the highly invasive lesior not because of the invasiveness per se was because these invasive, infiltrating c

were more likely to have recurred after previous treatment. In turn these recurrent lesions had had the opportunity to become extensive and to present more obstacles to cure than do less advanced lesions. Actually patients with highly invasive basal cell carcinoma of the eyelid are the ones most urgently in need of the microscopic control of excision provided by the chemosurgical technic. Some degree of keratinization was observed in eleven lesions (12.1 per cent) and pigment in two lesions (2.2 per cent) but neither keratinization nor pigmentation affected the response to chemosurgical treatment.

The effect of the site of origin on the prognosis of basal cell carcinoma of the eyelid is significant in that the more highly invasive lesions of the canthal regions are more likely to lead to serious complications than are the less invasive nodular carcinomas which commonly affect the upper and lower eyelids (Table XXIV)

TABLE XXIV
EFFECT OF SITE OF ORIGIN OF BASAL CELL CARCINOMA OF THE EYELID ON FIVE-YEAR END RESULTS

Site	*Number of Lesions*	*Successful Results Number*	*Per cent*
Lower lid	43	42	97 7
Upper lid	22	21	95 5
Inner canthus	20	17	85 0
Outer canthus	*6*	5	*83 3*

Therapeutic Results in Cases of Squamous Cell Carcinoma of the Eyelids

There was a total of eighteen cases of squamous cell carcinoma of the eyelids treated chemosurgically during the twelve year period ending six years prior to this writing The cancers were in all stages from early to advanced. One lesion had recurred after previous treatment and one patient developed regional metastasis.

The eighteen cases were divided into "indeterminate" and determinate groups. The indeterminate group included the cases of three patients who died of intercurrent disease before the end of five years without recurrence and one who was lost from observation before the end of five years without recurrence. The determinate group was composed of the case of the one patient who was unsuccessfully treated and the cases of the thirteen patients who were successfully treated (Table XXV)

TABLE XXV
FIVE-YEAR END RESULTS FOR SQUAMOUS CELL CARCINOMA OF THE EYELIDS

This series includes the cases of all patients with histologically proved squamous cell carcinoma, both early and advanced, previously untreated and recurrent, with and without metastasis, who were chemosurgically treated during the twelve year period ending six years prior to this writing

Total number of cases	18
Indeterminate group total number	4
Patients dead from other causes without recurrence	3
Patients lost from observation without recurrence	1
Determinate group, total number	14
Unsuccessful results, total number	1
Patients dead, cancer present at death	0
Patients lost from observation with cancer	1
Patients living with cancer	0
Successful results, patients free from cancer for five years or more	13
Five-year rate of cure (13 ÷ 14) × 100	92 9%

Therefore, after observation for five years or more successful results were obtained in thirteen of the fourteen determinate cases of squamous cell carcinoma of the eyelid. Hence, the five year rate of cure was 92.9 per cent. The primary lesion was eradicated in every case.

There were insufficient *numbers of cases* to provide *significant data regarding* the effects of various factors on prognosis. There was only one unsuccessfully treated case a rapidly growing, previously untreated squamous cell carcinoma of grade 3 malignancy size 11 mm., located on the lower eyelid at the junction with the cheek the cause of failure was submaxillary metastasis which was neglected by the patient until it had become inoperable. Attempted chemosurgical excision of the large mass which replaced the submaxillary salivary gland and invaded the mandible was of only palliative value. The primary lesion in this, as in every other case of squamous cell carcinoma of the eyelid, did not recur

The distribution of cases as regards the size of the lesions was as follows group A (average diameter under 1 cm), seven cases group B

(1 to 2 cm.), four cases group C (2 to 3 cm), two cases and group D (3 cm. or more), one case Examples of squamous cell carcinomas in group C (2 to 3 cm.) are illustrated in Figures 82 and 88 and one in group D is illustrated in Figure 94 Only one patient had received previous treatment. The distribution according to grade of malignancy was as follows grade 1, nine cases grade 2 three cases grade 3, two cases and grade 4 no cases. Nine lesions originated on the lower lid four on the upper lid one in the medial canthus and none in the lateral canthus.

Comparison of Results with Those of Other Authors

The excellent series of cases of basal cell carcinoma of the eyelid described by Magnussen[44] provides suitable data for comparison with the results obtained with chemosurgical treatment. Thus in his series of sixty determinate cases the five-year rate of cure was 85 per cent. In the series of ninety-one determinate cases in which the patients were treated by chemosurgery the rate of cure was 93 4 per cent. However in his series there were more cases in groups C and D (30 per cent as compared to 14 3 per cent in this series) but the proportion of lesions which had recurred after previous treatment was essentially the same in both series (31 7 per cent as compared to 33 per cent in this series)

There were no adequate series of squamous cell carcinoma of the eyelid for comparison

The chemosurgical method for the microscopically controlled excision of cancer of the eyelids provides a reliable and yet a conservative means of treatment The technic when properly employed does not endanger the function of the eye unless the eyeball actually is invaded or is surrounded by cancer Moreover in this series of 147 cases of carcinoma of the eyelids there were no deaths attributable to chemosurgical treatment.

CHAPTER 7

Carcinoma of the Extremities and Trunk

THE microscopic control of excision provided by the chemosurgical technic is just as important in the treatment of carcinoma of the extremities and trunk as it is in the treatment of cancer of the head and neck.[82] The reliability which may be attained by this method without the sacrifice of large amounts of normal tissues is of obvious economic value to the doctor or dentist with cancer on the fingers, to the manual laborer with cancer on the hand, or to almost anyone with cancer on the foot.

Because different problems are encountered in the chemosurgical treatment of cancer in various areas the subject is considered under the following headings (1) fingers (2) hand (3) arm (4) foot (5) leg, and (6) trunk.

Fingers

Sixty two per cent of the carcinomas of the fingers occurred in doctors or dentists (twenty six of forty two cases) The high incidence in these professions mostly was the result of exposure to roentgen rays from diagnostic machines. In doctors, who usually received their exposure during operative and manipulative procedures, the dorsum of the fingers and hands were most subject to carcinoma with the highest incidence being on the third and fourth fingers and on the mid-dorsum of the hand. In dentists, who received their exposure while holding dental films in the mouths of their patients, the damage was greatest on the thumbs, index fingers and middle fingers which structures were nearest the center of the beam of roentgen rays. However in dentists the damage to the index fingers was limited to their proximal portion because the tips were protected from the rays by the filtration afforded by the teeth, the alveolar ridge and the foil on the back of the dental film.

In the dentist whose livelihood depends on the function of his fingers, the conservatism made possible by the microscopic control of chemosurgical excision may be the factor which permits continuance of his profession. Thus, the preservation of the tip of the thumb (Figs. 97 and 98) or the function of the middle finger (Fig 99) may be of extraordinary economic importance. In the series of seven cases of cancer of the digits of dentists treated to date the distribution of lesions according to site were as follows distal part of thumb, four lesions over the proximal interphalangeal joint of the middle finger one lesion and proximal part of index finger two lesions.

Physicians, particularly those who specialize in surgery also are dependent upon the function of their fingers, and the improved chance of preserving useful digits afforded by the chemosurgical technic is an important consideration to them. Often the carcinomas arise over interphalangeal joints and in such cases the conservatism of the chemosurgical technic is particularly valuable (Fig 100) The distribution of squamous cell carcinomas of the fingers of the physicians treated to date was as follows thumb one lesion index finger four lesions middle finger six lesions fourth finger, five lesions and fifth finger three lesions. There was one basal cell carcinoma produced by roentgen exposure.

The endarteritis hyperkeratosis, atrophy and other changes produced by roentgen rays may impair the healing process after chemosurgical excision of cancer The rate of healing is slightly slower than in unirradiated tissues and the epithelium over the resultant scar may be

1

thinner and more subject to trauma than in patients who have not sustained radiation damage However in the process of removing the cancer enough of the most heavily irradiated



Fig. 97 (A) Squamous cell carcinoma, grade 1 which had arisen on the thumb of a dentist who had occasionally held dental films in the mouths of his patients over a period of thirty five years. (B) Granulation tissue after chemosurgical excision. The cancer invaded the periosteum of the tip of the phalanx but did not involve the bone (Fig 98) (C) Healed lesion. The patient was able to continue his dental practice and even the sport of bowling There was no recurrence after fourteen years.

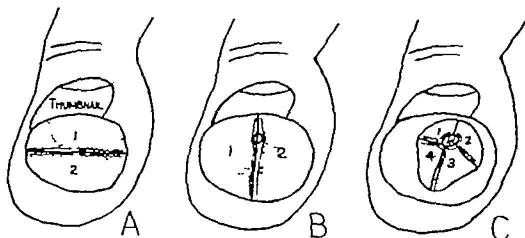


Fig 98 Maps showing the origin of specimens removed on successive days from the lesion pictured in Figure 97 The straight and wavy lines at the edges of the specimens indicate that the edges were marked with mercurochrome and India ink respectively to aid in orientation. Stippled areas represent cancer located microscopically in frozen sections. The cross hatched areas in B and C represent the tip of the phalangeal bone.

superficial tissues usually is removed to reach the better vascularized tissues at a deeper level accordingly the healing ordinarily is quite satisfactory and the digits usually function well. If large areas of epithelium must be removed, split thickness grafts may be advisable especially if the granulating wound is over a joint the motion of which might be limited by a constricting scar Cancers of the fingers not produced by roentgen rays often are the result of long exposure to the ultraviolet rays of the sun. These rays have less penetrating power

and hence do not appreciably damage the healing qualities of the underlying tissues (Fig 101)

When the dressings are applied to the fingers care must be exercised to avoid placing the in one case there was involvement of bone which was not recognized this way Therefore, if there is any doubt the bone should be subjected to microscopic section.

If in the treatment of cancer of the end of

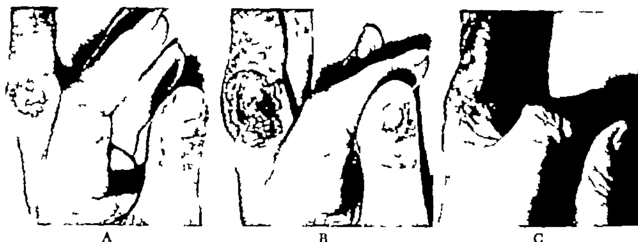


Fig 99 (A) Squamous cell carcinoma, grade 3 malignancy on the middle finger of a dentist who occasionally had held dental films in the mouths of his patients. There also was severe radiodermatitis of the distal part of the thumb. (B) Granulation tissue after chemosurgical excision of the cancer which approached but did not enter the interphalangeal joint. The crusts, scales and loose nail were dissected from the thumb. (C) Healed lesion. There was practically no impairment of function of the middle finger and the thumbnail had regrown. There was no recurrence after six years.



Fig 100. (A) Squamous cell carcinoma, grade 2, on the second and third digits of a physician who had been exposed repeatedly to a diagnostic x ray machine about twenty-five years before. There also was a keratosis on the dorsum of the fourth digit. (B) Granulation tissue after chemosurgical excision of the three lesions. (C) Healed lesions. There was practically no impairment of function. There was no recurrence when the patient died of other causes after seven years.

adhesive tape around the entire finger because if the edema is appreciable the circulation may be cut off

Usually carcinomatous involvement of the phalangeal bone is grossly detectable However a finger a cancer free plane is reached at the level of an interphalangeal joint, it is advisable to carry fixation into the body of the phalangeal bone rather than leave the surface of the joint exposed. Otherwise the poorly vascularized

articular cartilage prevents healing The phalangeal bone should be cut off flush with or slightly below the level of the soft tissues. This allows a pad of soft tissues to pull over the end of the bone as the wound heals and the scar contracts. The resultant stump is satisfactory carcinoma on other exposed parts of the body ultraviolet irradiation from the sun was the most potent external causative agent

Some cancers may present a considerable protruding mass and yet not penetrate to the level of the tendons bones and joints (Fig



Fig 101 (A) Squamous cell carcinoma grade 2 malignancy (B) Granulation tissue after chemosurgical excision. (C) Palmar aspect showing that besides involving the index finger there was an extension into the palm at the base of the middle finger (D) Healed lesion. Flexion was slightly restricted but the patient was able to use the finger for grasping There was no recurrence after six years.

from both a functional and cosmetic standpoint.

Hand

In contrast with cancer of the fingers, only a very small proportion of cancers of the dorsum of the hand develop from damage by roentgen rays. Thus, the number of doctors who developed cancer after having received roentgen irradiation was four (5 1 per cent of the seventy-eight cases of squamous cell carcinomas of the hand) In common with squamous cell

102) Other cancers may skirt around and spare important structures which to clinical examination would seem to be extensively involved (Fig 159) Still others may extend around tendons making their exposure necessary but not necessarily destroying their function because granulation tissue and epithelium may cover over and preserve the function of the fixed tendons (Fig 103) In such cases it is not known whether the tendons remain intact or are gradually replaced by new fibers but, in either event, they do remain functional. The

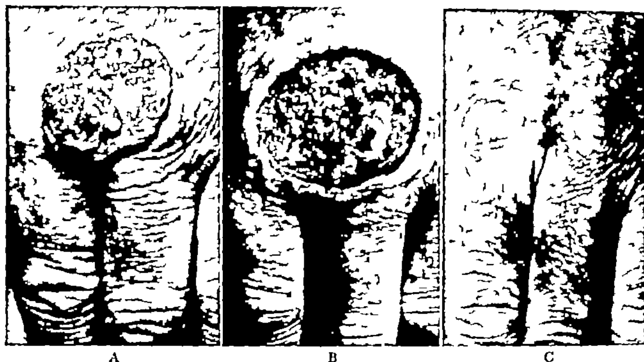


Fig 102. (A) Squamous cell carcinoma, grade 2 malignancy It had recurred after two surgical excisions. (B) Granulation tissue after chemosurgical excision. (C) Healed lesion. There was no recurrence after five years.



Fig 103 (A) Squamous cell carcinoma, grade 3 malignancy The neoplasm had recurred after three courses of roentgen therapy (B) Granulation tissue after chemosurgical excision. The exposed tendons soon became covered with granulation tissue and epithelium, their extensor function was retained. (C) Healed lesion. The central dark area is at the point where an adherent scale had been pared off with slight bleeding. There was no recurrence after six years.

th of tendon that will be covered by granu n tissue varies from one to about eight imeters, there being a considerable differ between individuals in this respect

ancerous outgrowths which extend deeply the hand may be followed down between tendons and bones with accurate micro- ic visualization by means of the chemo- ical technic. By preserving all uninvolved ctures it often is possible to salvage a useful d despite extensive involvement (Fig 101)



. 104 (A) Squamous cell carcinoma, grade 1 malignancy which arose in a scar from a burn sustained age two. The neoplasm had recurred after numerous treatments with radium and then with caustics. Granulation tissue after chemosurgical excision of the cancer which invaded the second and third tacarpal bones necessitating removal of the middle two-thirds of each. (C) Healed lesion. The scar tis- held the tissues together firmly with the result that excellent gripping function was retained. There was no recurrence when the patient died of other causes after five years.

e firm but pliable scars which follow chemo- gical treatment tend to hold the tissues to- her in such a way that considerable lifting d grasping function is retained. If the car oma is found to extend through the hand to olve a considerable area of the palmar sur e it may prove advisable to amputate the nd as was done in one case in this series.

The constant motion and repeated trauma tained by cancers located on the hand have tendency to increase the incidence of metas- is. Therefore close observation and early section of enlarged axillary nodes is indi cated If the primary lesion is large and of a fairly high degree of malignancy prophylactic dissection of the axillary contents may be indi cated. If the axillary nodes are massive and fixed the only hope of cure lies in amputation of the fore quarter

Arm

Carcinoma on the arm above the wrist is rare Unless the cancer invades into large ar teries or into nerves, it may be chemosurgically excised without complications regardless of size (Fig 105)

Foot

Carcinoma of the foot is not common, and all of the cases in this series were of the squa mous cell type. The microscopic control of ex cision afforded by the chemosurgical technic makes possible the removal of neoplasms which have extended into the interstices between the bones of the foot or ankle. In such cases, the wounds heal with scars which give adequate support for good function (Fig 158) Con

nderable amounts of tissue may be removed from the anterior part of the foot (Fig 106) or from the heel (Fig 107) without appreciable impairment of function. Postchemosurgical scars on the bottom of the feet usually stand up well under weight bearing

for them to break down. In no case has a po chemosurgical scar led to carcinoma.

Trunk

The most common variety of carcinoma the trunk is the superficial basal cell type whi



Fig 105 (A) Basal cell carcinoma on the ulnar side of the elbow. The lesion had recurred after numer ous treatments with electrodessication and caustics. (B) Healed lesion after chemosurgical excision. There was no recurrence after nine years.

Leg

Many lesions on the leg are squamous cell carcinomas originating in chronic ulcers from trauma (Fig 108) or from burns (Fig 109). Usually the cancers are not in the vicinity of large nerves or arteries, and the removal of neoplasms of large size can be accomplished without difficulty. The scars after chemosurgical treatment are softer and better vascularized than burn scars and there is no tendency

shows a strong tendency to be erythematous and to be multiple (Fig 110). These neoplasms often spread to involve very large areas. In such cases it is unnecessary to section the entire central portion because the neoplasm is so uniformly superficial. However it is advisable to section the entire periphery because the neoplasm often is found to extend farther than expected at some points. Although this variety of cancer almost always remains superficial for years it occasionally may suddenly develop into



Fig 106. (A) Squamous cell carcinoma, grade 4 malignancy The neoplasm had arisen in a chronically ulcerated scar which followed amputation in a train accident thirty five years previously (B) Granulation tissue after chemosurgical excision of the cancer which invaded the metatarsal bones. Enlarged inguinal nodes were dissected but were found not to contain cancer (C) Healed lesion. The patient got around on crutches and this foot, the other leg having been amputated. There was no recurrence after five years.

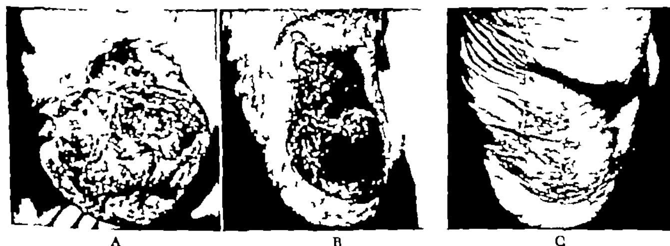


Fig 107 (A) *Squamous cell carcinoma of the heel, grade 3 malignancy* The neoplasm and a number of plantar and palmar keratoses were thought to be a result of arsenical medication for psoriasis. The cancer had recurred after electrosurgical excision and after surgical excision and grafting (B) Granulation tissue after chemosurgical excision and partial healing One metastatic node was found on dissection of the inguinal region (C) Healed lesion The patient could walk on the foot without difficulty There was no recurrence in the primary or secondary regions when the patient died of other causes after five years.

a more rapidly growing deeply invasive type of basal cell carcinoma. In this series three patients with multiple superficial basal cell carcinomas had had psoriasis and one had received prolonged treatment with arsenic for this disease The possible etiologic relationship between psoriasis and arsenic treatment on the one hand and superficial basal cell carcinoma of the trunk and extremities on the other has been noted by others.

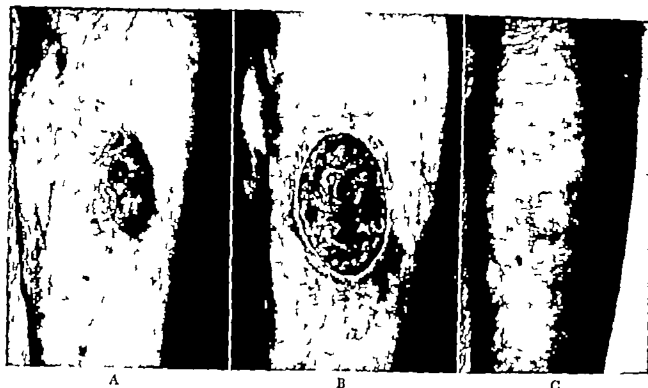


Fig 108. (A) Squamous cell carcinoma, grade 3 malignancy over the tibial crest. The neoplasm arose in a chronic ulcer which followed trauma to the skin four years previously (B) Granulation tissue after chemosurgical excision. The cancer extended for an unexpectedly great distance at four points at the periphery (C) Healed lesion. There was no recurrence after eight years.



Fig 109 (A) Squamous cell carcinoma, grade 2 malignancy The neoplasm had originated in a scar from a fire burn sustained fifty years previously It had recurred after excision and grafting on three occasions. (B) Granulation tissue after chemosurgical excision of the cancer which extended into the femur and for a considerable distance under the grafted surface. (C) Healed lesion. There was no recurrence after six years.

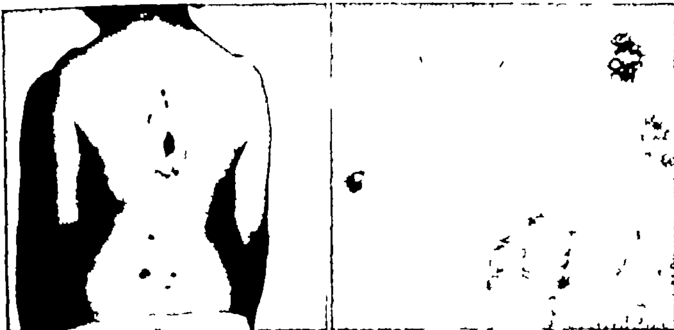


Fig. 110 (A) Multiple superficial erythematous basal cell carcinomas of the trunk. There were thirty six lesions on the front and back of the trunk. (B) Close up view of the interscapular region. Some of the lesions contained melanin pigment (C) Granulation tissue after chemosurgical excision. (D) Healed lesions. There was no recurrence after six years although seven new ones appeared at different sites.

Carcinoma of the trunk occasionally is of a more highly invasive basal cell type or of the squamous cell type and these usually can be removed chemosurgically without complications regardless of size (Fig 111) In some cases the carcinoma has been followed down around the spinous processes and the posterior surfaces of the vertebrae. On the abdominal wall the neoplasm may extend to the peritoneum, a complication which prevents completion of treatment because of the danger of peritonitis.

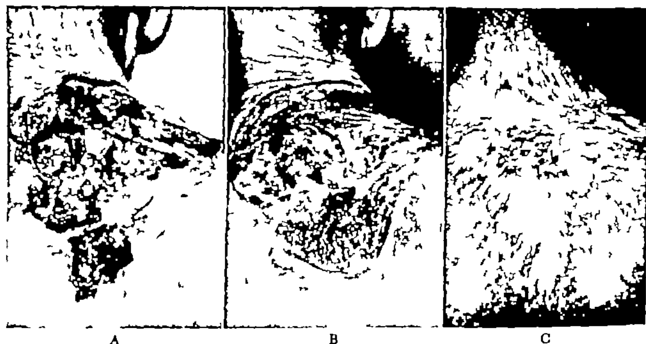


Fig 111 (A) Basal cell carcinoma in the posterior nuchal and scapular regions. It had recurred after many excisions and many roentgen treatments over a period of thirty years. (B) Granulation tissue after chemosurgical excision. The cancer eroded the spines of the seventh cervical and first two dorsal vertebrae. (C) Healed lesion. The atrophy and depigmentation are results of the previous irradiation. There was no recurrence after five years.

Among such cases however there may be instances in which a small residual focus may be excised surgically and the defect closed immediately In one instance a carcinoma of the abdominal wall extended into the mucosa of the bladder a fistula developed and, although this could readily have been repaired, the patient had another area of cancer which eroded through the peritoneum so treatment had to be discontinued Neoplasms which erode through the pleura also may present difficult therapeutic problems However in a number of cases portions of ribs and intercostal muscles have been removed chemosurgically without entering the pleural cavity The swelling incident to the chemical treatment tends to push the pleura away from the treated area providing an extra margin of safety

Therapeutic Results in Cases of Basal Cell Carcinoma of the Extremities and Trunk

Ninety six basal cell carcinomas were chemosurgically excised in the twelve year period which ended six years prior to this writing The cancers were in all stages from early to advanced. Previous unsuccessful surgical or radiation treatment had been received in 10 7 per cent of the cases. There were no metastases.

The 96 cases were divided into "indeterminate and "determinate" groups. The indeterminate group included the cases of eight patients who died of intercurrent disease before the elapse of five years without recurrence and the cases of four patients who were lost from observation before the end of the five year period without recurrence. The determinate group included the cases of eighty four succes-

fully treated patients there were no cases in which treatment was unsuccessful (Table XXVI)

TABLE XXVI

FIVE-YEAR END RESULTS FOR BASAL CELL CARCINOMA OF THE EXTREMITIES AND TRUNK

This series includes the cases of all patients with histologically proved basal cell carcinoma both early and advanced previously untreated and recurrent who were chemosurgically treated during the twelve year period ending six years prior to this writing

Total number of cases	96
Indeterminate group total number	12
Patients dead from other causes without recurrence	8
Patients lost from observation without recurrence	4
Determinate group total number	84
Unsuccessful results, total number	0
Patients dead, cancer present at death	0
Patients lost from observation with cancer	0
Patients living with cancer	0
Successful results, patients free of cancer for five years or more	84
Five-year rate of cure (84 ÷ 84) × 100	100%

Therefore, the five year cure rate in eighty four determinate cases of basal cell carcinoma of the extremities and trunk was 100 per cent.

The effect of the size of the lesion on prognosis was nil as far as the statistics in this series of basal cell carcinomas is concerned because all of the patients were cured regardless of the size of the lesion. However it is obvious that larger lesions have a greater chance of eroding into vital structures such as the peritoneum, the pleura, the axillary artery or the inguinal artery and this in turn would reduce the chance of cure despite the microscopic control of excision afforded by the chemosurgical technic This series included an appreciable number of large lesions as indicated by the following data on the size of the lesions as measured at the initial clinical examination group A (under 1 cm. in average diameter) twenty five cases group B (1 to 2 cm.) thirty four cases group C (2 to 3 cm.) ten cases and group D (over 3 cm) fifteen cases. Although some of the lesions were very extensive as exemplified by figures 105 and 111 none affected vital structures whose involvement might have precluded a successful result.

The effect of previous treatment on prognosis is not indicated by the data on the present series because all of the lesions were successfully treated regardless of whether or not there had been previous treatment. This indicates the particular value of the chemosurgical technic in the treatment of recurrent lesions. However it is obvious that the circumstance of previous treatment might be an adverse factor in prognosis if the delay occasioned by the unsuccessful treatment allowed the carcinoma to extend into vital structures.

The effect of the histologic degree of invasiveness is not indicated by the present data because of the uniform success in treatment regardless of the degree of invasiveness. Basal cell carcinomas of the extremities and trunk tend to be less invasive than those in the head and neck region thus only 10 7 per cent of the lesions were classified as highly invasive Obviously however the highly invasive lesions would have an increased tendency to invade vital structures but this complication did not occur in this series. No adverse effect was exerted by keratinization, which was present in 3 6 per cent of the carcinomas or by melanin pigmentation, which was present in 6 per cent of the lesions.

The effect of the site of origin on prognosis was not indicated by the present data because of the regularly successful outcome in all cases of basal cell carcinoma of the extremities and trunk. However advanced carcinomas located over the peritoneum the pleura or the large arteries obviously would be more likely to preclude a successful result by the involvement of these vital structures than would advanced neoplasms not so located. The distribution of basal cell carcinomas in the various areas of the extremities and trunk was as follows trunk seventy-eight lesions arm two lesions hand one lesion finger one lesion and leg two lesions.

Therapeutic Results in Cases of Squamous Cell Carcinoma of the Extremities and Trunk

One hundred squamous cell carcinomas of the extremities and trunk were chemosurgically excised during the twelve year period which

ended six years prior to this writing The cancers were in all stages from early to advanced. Previous unsuccessful treatment by radiation or surgical excision had been received by 40 0 per cent of the patients. There were regional metastases in eleven cases.

The 100 consecutive cases were divided into indeterminate and "determinate groups The indeterminate group was composed of the cases of eighteen patients who died of other causes before the elapse of five years without recurrence of the cancer, and the case of one patient who was lost from observation without recurrence The determinate group included the cases of eleven patients who were unsuccessfully treated and the cases of seventy patients who were successfully treated (Table XXVII)

TABLE XXVII

FIVE-YEAR END RESULTS FOR SQUAMOUS CELL CARCINOMA OF THE EXTREMITIES AND TRUNK

This series includes the cases of all patients with histologically proved squamous cell carcinoma, both early and advanced, previously untreated and recurrent, with and without metastasis, who were chemosurgically treated during the twelve year period ending six years prior to this writing

Total number of cases	100
Indeterminate group total number	19
Patients dead from other causes without recurrence	18
Patients lost from observation without recurrence	1
Determinate group total number	81
Unsuccessful results, total number	11
Patients dead, cancer present at death	9
Patients lost from observation with cancer	2
Patients living with cancer	0
Successful results, patients free from cancer for five years or more	70
Five-year rate of cure (70 + 81) X 100	86 4%

Therefore the rate of cure after five or more years of observation in the eighty-one determinate cases of squamous cell carcinoma of the extremities and trunk was 86 4 per cent.

There were only two cases in which the primary lesion was the cause of failure to eradicate the disease In other words in seventy nine of eighty-one determinate cases the primary lesion was successfully treated (97.5 per cent)

The effect of the size of the lesion on prognosis was considerable (Table XXVIII) The

TABLE XXVIII

EFFECT OF SIZE OF SQUAMOUS CELL CARCINOMA OF THE EXTREMITIES AND TRUNK ON FIVE-YEAR END RESULTS

Group	*Average Diameter Cm*	*Number of Lesions*	*Successful Results Number*	*Per cent*
A	under 1	9	9	100 0
B	1 to 2	32	30	93 8
C	2 to 3	13	12	92 3
D	3 or more	27	19	70 4

chief reason for the adverse effect of large size of the primary cancer was the greater incidence of metastasis. Thus, in this series the eleven cases in which unsuccessful results were associated with metastasis most of the cancers were large eight were classified in group D (diameter 3 cm or more), one was in group C (diameter 2 to 3 cm.) and two in group B (diameter 1 to 2 cm.) There were two cases in which failure was due to the extensiveness of the primary lesion although there was no metastasis in one of these cases the cancer of the dorsum of the hand eroded through the palmar surface to such an extent that surgical amputation of the hand was carried out (with a succesful result), in the other case the extensive cancer of the abdominal wall was found to invade the peritoneum so treatment was discontinued. Examples of squamous cell carcinomas of various sizes are illustrated as follows group B in Figures 97 99 and 100 group C in Figure 100 group D in Figures 101 102, 103 104 106 107 108 and 109

The effect of previous treatment on prognosis was appreciable as indicated by the fact that only 78 1 per cent of the thirty two patients with previously treated lesions were cured while 91 8 per cent of the forty nine patients who had not received previous treatment were cured. The main reason for failure in the cases with recurrent cancer was the delay which allowed the neoplasms to become more extensive and either to metastasize or to involve structures which precluded eradication of the primary lesion by chemosurgical treatment. However the fact that 78 1 per cent of the recurrent

lesions were eradicated by chemosurgical treatment bespeaks the effectiveness of this method in complicated cases.

The effect of the grade of malignancy on prognosis in cases of squamous cell carcinoma of the extremities and trunk was definite (Table XXIX) There was a drop in the rate of cure

TABLE XXIX
EFFECT OF HISTOLOGIC GRADE OF MALIGNANCY OF SQUAMOUS CELL CARCINOMA OF THE EXTREMITIES AND TRUNK ON FIVE-YEAR END RESULTS

Grade	Number of Lesions	Successful Results Number	Per cent
1	32	32	100 0
2	31	27	87 1
3	15	9	60 0
4	3	2	66 7

from 100 per cent in the patients with grade 1 carcinomas to 60 0 per cent in those with grade 3 lesions. Since there were only three cancers in the grade 4 group the 66.7 per cent cure rate is not very significant. The greater tendency toward metastasis accounted for most of the poor results in the patients with the more malignant lesions.

The effect of site of origin on prognosis in squamous cell carcinoma of the extremities and trunk was significant (Table XXX) The lower

TABLE XXX
EFFECT OF SITE OF ORIGIN OF SQUAMOUS CELL CARCINOMA OF THE EXTREMITIES AND TRUNK ON FIVE-YEAR END RESULTS

Site	Number of Lesions	Successful Results Number	Per cent
Fingers	19	18	94 7
Hand	34	29	85 3
Arm	2	2	100 0
Foot and toes	9	6	66 6
Leg	7	6	85 7
Trunk	10	9	90 0
All sites	81	70	86 4

rates of cure for cancer of the hands and feet reflect the adverse influence of trauma and motion on the incidence of metastasis. Only one of the carcinomas of the arm, leg or trunk metastasized, and only *one* carcinoma of the fingers metastasized Perhaps the small siz the lymphatics in the fingers plus the relati small size of the neoplasms in this loca accounts for the fewer metastases and hence higher rate of cure.

The effect of metastasis on prognosis profound Thus, in the group of eleven pati with metastasis there were only two succe results (18 2 per cent) while in the grou seventy patients without metastasis there sixty-eight successful results (97 1 per cent)

In six cases the axillary or inguinal n were surgically dissected and successful re were obtained in two cases with inguinal me tasis. The other nodes were excessively larg unfavorably located with the result that re rence developed. Shoulder girdle amputa which was recommended to two patients refused by both though one later agreed h ever, by that time there was so much inv ment of the chest wall that complete rem was not feasible One patient with axillary tastasis was apparently cured by resectio the shoulder girdle by Dr K. E. Lemmer since the patient died of other causes after years, this case cannot be classified as a cessful outcome In one case palpable axi nodes were resected but the enlargement because of lymphadenitis and not cancer prophylactic dissections were carried out in series. However in cases in which the ca is large and highly malignant there occasio may be justification for axillary or inguinal sections in the absence of palpable nodes.

In two cases there were metastatic foci i lymphatic vessels adjacent to the primary le In one of these cases, that of a patient carcinoma on the dorsum of the hand t were numerous satellite nodules affecting n of the back of the hand (Fig 165) subseq axillary metastases were not controlled by lary dissection and roentgen therapy In other case that of a dentist with carcin which invaded most of the thumb, there embolic foci in the lymphatics to the upper of the wrist axillary dissection failed to co the metastases and, as previously mentio the recommended amputation of the fore q ter was refused until it was too late. From experience in these two cases it is obvious

embolic foci in the lymphatics adjacent to a carcinoma indicate a very unfavorable prognosis and they call for immediate radical measures to forestall spread beyond the axillary or inguinal nodes.

In all cases of squamous cell carcinoma of the extremities very close observation of the regional nodes is indicated. In the present series there were a few patients who failed to return as instructed and they developed inoperable masses before reporting for examination. More vigorous measures now being used to assure regular check up visits should prevent future failures from this cause.

Comparison of Results with Those of Other Authors

There are no really adequate statistics in the literature concerning the results of treatment of carcinoma of the extremities and trunk. Magnussen's[3] series of basal cell carcinoma included only six determinate cases of which five were cured. This yields a five-year cure rate of 83.3 per cent as compared to 100 per cent in the present series of eighty-four determinate cases in which chemosurgical treatment was employed.

Similarly with squamous cell carcinoma, Magnussen's series included only seven determinate cases with a five year cure rate of 57.1 per cent. In the present series of eighty-one determinate cases in which chemosurgical treatment was used, the five year cure rate was 86.4 per cent.

Thus, for both basal and squamous cell carcinoma of the extremities and trunk the results obtained with the chemosurgical treatment excelled those obtained in a similar but much smaller series in which the patients were treated with ordinary surgical and radiation technics. Not only were the rates of cure high, but the unusual degree of conservatism allowed preservation of useful structures. Also there was only one death during chemosurgical treatment it was the result of coronary occlusion and was not considered to have been due to the operation.

CHAPTER 8

Carcinoma of the Skin A Summary of Therapeutic Results with Comments

THE preceding chapters have dealt with the results obtained by the chemosurgical treatment of patients with cancers in specific areas of the skin. The purpose of this chapter is to summarize and comment on the therapeutic results in cases of basal cell carcinoma and squamous cell carcinoma of all areas of the skin with the exception of the penis vulva and anus which areas are considered in subsequent chapters.[41,44,45,46,74] The data are given in sufficient detail to permit ready comparison with the results of other authors.

This series is composed of 1,554 consecutive cases of microscopically proved, cutaneous carcinoma in which chemosurgical treatment was employed during the twelve year period ending six years prior to this writing There were 1 071 basal cell carcinomas and 483 squamous cell carcinomas. The neoplasms were in all stages from early to advanced actually there was an unusually large proportion of advanced lesions because many of the patients came from other parts of the country for chemosurgical treatment of cancers which had failed to respond to the usual surgical and radiologic treatments. One third of the patients had received previous unsuccessful treatment by irradiation or surgery A few of the patients had two or more cancers which arose independently in different areas of the skin however since each neoplasm constituted an individual therapeutic problem each was considered to constitute a separate case.

Inasmuch as there is a considerable difference between the clinical behavior of basal cell carcinoma and that of squamous cell carcinoma the results of the chemosurgical treatment of each type of neoplasm is considered separately The series includes a relatively small number of cases of mixed basal and squamous cell carcinomas and a few cases of carcinoma with intermediate histologic characteristics. These have been placed in either the basal cell or the squamous cell categories depending upon which type was predominant or most nearly approached.

Therapeutic Results in Cases of Basal Cell Carcinoma of the Skin

There was a total of 1 071 cases of basal cell carcinoma treated chemosurgically during the twelve year period which ended six years prior to this writing The cancers were in all stages from early to advanced. More than one third (34 1 per cent) of the patients had received previous surgical or radiologic treatment. There were no metastases from carcinomas which were purely basal cell in type. The diagnosis was established microscopically in every case.

The 1 071 cases of basal cell carcinoma of the skin were divided into "indeterminate" and "determinate" groups. The indeterminate group of 289 cases included the cases of 260 patients who had no cancer when they died of other causes before the expiration of five years, and the cases of twenty nine patients who were lost from observation before the end of the five year period but who were without recurrence when last seen The 782 cases in the determinate group included the cases of fourteen patients who were unsuccessfully treated and the cases of 768 patients who were successfully treated (Table XXXI)

Therefore, successful five year end results

TABLE XXXI

FIVE-YEAR END RESULTS FOR BASAL CELL CARCINOMA OF THE SKIN

This series includes the cases of all patients with histologically proved basal cell carcinoma, both early and advanced, previously untreated and recurrent who were chemosurgically treated during the twelve year period ending six years prior to this writing

Total number of cases	1,071
Indeterminate group, total number	289
Patients dead from other causes without recurrence	260
Patients lost from observation without recurrence	29
Determinate group total number	782
Unsuccessful results, total number	14
Patients dead, cancer present at death	11
Patients lost from observation with cancer	3
Patients living with cancer	0
Successful results, patients free from cancer for five years or more	768
Five-year rate of cure (768 ÷ 782) × 100	98 2%

were obtained in 98 2 per cent of the 782 cases in the determinate group

In the following paragraphs data are given concerning the prognostic influence of such factors as the size of the lesion, previous unsuccessful treatment, the histologic degree of invasiveness and the site of origin. Not only is this material useful in estimating prognosis in an individual case but it also serves to indicate the kinds of cases included in this series. The latter consideration is of special interest to workers who are interested in comparing their results with those obtained by means of chemosurgical treatment.

The effect of the size of the lesion on prognosis is relatively slight unless the carcinoma exceeds 3 cm. in average diameter (Table XXXII) Thus there was only one unsuccessfully treated case in each of groups A (diameter under 1 cm.) B (diameter 1 to 2 cm.) and C (diameter 2 to 3 cm.) while there were eleven in the numerically smaller group D (diameter 3 cm. or more) However extensiveness per se is not a contraindicatory factor for chemosurgical treatment of basal cell carcinoma of the skin unless the neoplasm has extended into some vital structure, such as the brain, carotid artery or the jugular vein. Actually, a considerable number of patients with extremely advanced carcinomas were chemosurgically treated, and in most of these successful results were obtained. However in some patients treatment was discontinued because of invasion through the skull into the vital portions of the brain (three patients), some for various reasons did not stay for completion of treatment (seven patients) while some had cancers which were found to be too advanced to justify complete removal in consideration of the patients advanced age and poor general condition (four patients) Incidentally the sizes referred to in this book are the average diameters of the cancers as measured at the initial clinical examination the actual size as demonstrated during the course of chemosurgical excision often was much larger

TABLE XXXII

EFFECT OF SIZE OF BASAL CELL CARCINOMA OF THE SKIN ON FIVE-YEAR END RESULTS

Group	Average Diameter Cm	Number of Lesions	Successful Results Number	Per cent
A	under 1	305	304	99 7
B	1 to 2	294	293	99 7
C	2 to 3	95	94	98 9
D	3 or more	88	77	87 5

The effect of previous treatment on prognosis is appreciable as indicated by the five-year cure rate of 95 6 per cent in the group of 267 patients with recurrent lesions as compared to the rate of 99 4 per cent in the group of 515 patients who had not received previous treatment. However the efficacy of the chemosurgical method in recurrent lesions is indicated by the cure rate of 95 6 per cent which was attained despite the circumstance of recurrence. Actually patients with recurrent cancer are those in whom chemosurgical treatment is most urgently needed, but the delay occasioned by the previous ineffective treatment occasionally may allow the neoplasm to become so extensive that its cure is not feasible.

The effect of the degree of invasiveness on prognosis is definite. Thus, the five year cure rate in the group of 473 patients with highly invasive basal cell carcinomas was 97 0 per cent as compared to 100 per cent in the group of 309 patients with relatively noninvasive carcinomas. However this does not mean that the chemosurgical method is not highly effec

tive in the treatment of highly invasive lesions. Quite the contrary the microscopic control provided by the chemosurgical method often is most needed by patients with infiltrative neoplasms which have a tendency to spread in unpredictable directions for unexpectedly great distances. The chief reason for the lower rate of cure is that the invasive neoplasms are the ones most likely to have recurred after other treatment and to have had time to become so widespread that cure was not feasible.

Keratinization was observed in 14 8 per cent of all basal cell carcinomas in this series while melanin pigment was observed in 1.9 per cent of the lesions Neither keratinization nor pigmentation had an appreciable effect upon the response to chemosurgical treatment. By way of contrast, keratinizing basal cell carcinoma (basal-squamous cell carcinoma, or spinobasal cell carcinoma) often exhibits considerable resistance to irradiation. Most of the keratinizing basal cell carcinomas in this series were classified as highly invasive.

Classification of the basal cell carcinomas according to the degree and direction of differentiation is of considerable academic interest. However since there often is more than one histopathologic type present in a given lesion and since the degree of invasiveness may vary widely within a given type it has seemed more significant to simply designate whether the lesion had a relatively high or relatively low degree of invasiveness. There were numerous instances of intermediate degrees of invasiveness but for maximum simplicity an arbitrary mid point was chosen and the number of categories was limited to two Of course all the benign epithelial neoplasms such as trichoepithelioma (epithelioma adenoides cysticum or multiple benign cystic epithelioma) syringoma, cylindroma, etc. were excluded from this series.

The effect of site of origin on prognosis in basal cell carcinoma of the skin is considerable. Neoplasms which were located on surfaces away from orifices exhibited an excellent prognosis as indicated by the five year cure rate of 100 per cent for basal cell carcinoma of the face scalp, neck, extremities and trunk. The cure rate for basal cell carcinoma of the nose was nearly as high (97 7 per cent) On the other hand the rates of cure for carcinoma of the ears and eyelids were only 94.2 per cent and 93 4 per cent respectively (Table XXXIII)

TABLE XXXIII
EFFECT OF SITE OF ORIGIN OF BASAL CELL CARCINOMA OF THE SKIN ON FIVE-YEAR END RESULTS

Site	Number of Lesions	Successful Results Number	Successful Results Per cent
Face and head	338	338	100 0
Nose	217	212	97 7
Ear	52	49	94 2
Eyelids	91	85	93 4
Extremities and trunk	84	84	100 0
All sites	782	768	98 2

The lower rate of cure in cases of basal cell carcinoma of the ear was largely accounted for by the closeness to vital structures such as the carotid artery jugular vein inner ear, transverse venous sinus and the brain. The three unsuccessfully treated patients had carcinomas which arose in the concha canal and postauricular sulcus which areas were relatively close to the underlying vital structures. In two of the patients the neoplasm invaded through the cranium to the dura, and in one case the cancer invaded around the carotid vessels.

The somewhat lower rate of cure in the series of basal cell carcinoma of the eyelids was the result of failures for several reasons. In two cases the patients refused enucleation which would have been necessary to eradicate their neoplasms In three cases early in the series some of the numerous ramifications of the extensive carcinomas were missed. In one case in which there was extensive invasion of the ethmoid sinuses the patient died of meningitis which resulted from penetration of the cribriform plate.

Therapeutic Results in Cases of Squamous Cell Carcinoma of the Skin

There was a total of 483 cases of squamous cell carcinoma treated chemosurgically during the twelve year period which ended six years prior to this writing The cancers were in all stages from early to advanced Nearly one third of the patients (32 0 per cent) had received previous surgical or radiation treatment. Metas-

tases were present in 12.4 per cent of the patients. The diagnosis was established microscopically in every case.

The 483 cases of squamous cell carcinoma of the skin were divided into "determinate" and "indeterminate" groups. The indeterminate group of 127 cases was composed of the cases of 124 patients who died of other causes without recurrence and the cases of three patients who were lost from observation before the elapse of five years and who were without recurrence when last seen. The determinate group of 356 cases was composed of the cases of fifty four patients with unsuccessful results and the cases of 302 patients with successful results (Table XXXIV)

TABLE XXXIV

FIVE-YEAR END RESULTS FOR SQUAMOUS CELL CARCINOMA OF THE SKIN

This series includes the cases of all patients with histologically proved squamous cell carcinoma, both early and advanced, previously untreated and recurrent, with and without metastasis, who were chemosurgically treated during the twelve year period ending six years prior to this writing

Total number of cases	483
Indeterminate group, total number	127
Patients dead from other causes without recurrence	124
Patients lost from observation without recurrence	3
Determinate group, total number	356
Unsuccessful results, total number	54
Patients dead, cancer present at death	44
Patients lost from observation with cancer	10
Patients living with cancer	0
Successful results, patients free from cancer for five years or more	302
Five-year rate of cure (302 ÷ 356) × 100	84 8%

Therefore, successful five year end results were attained in 84.8 per cent of the cases of squamous cell carcinoma in the determinate group Most of the unsuccessful results were due to metastasis because the primary lesion presumably was eradicated in 94 0 per cent of the cases.

The effect of the size of the lesion on prognosis is notable as indicated by the drop in the rate of cure from 100 per cent in group A (diameter under 1 cm.) to 51.2 per cent in group D (over 3 cm.) (Table XXXV) The

TABLE XXXV

EFFECT OF SIZE OF SQUAMOUS CELL CARCINOMA OF THE SKIN ON FIVE-YEAR END RESULTS

Group	*Average Diameter Cm.*	*Number of Lesions*	*Successful Results Number*	*Per cent*
A	under 1	112	112	100 0
B	1 to 2	117	111	94 7
C	2 to 3	43	36	83 7
D	3 or more	84	43	51 2

cause of failure was the presence of uncontrollable metastasis in thirty-seven cases, the invasion of vital structures in nine cases, too extensive involvement for complete removal in seven cases and death of coronary occlusion during treatment in one case. Regardless of the cause of failure the great majority of the unsuccessfully treated patients had large lesions. Thus, of the thirty seven patients with metastasis twenty-six had group D lesions while six had group C lesions (diameter 2 to 3 cm.) and five had group B lesions (diameter 1 to 2 cm.) Similarly the nine cancers which invaded vital structures were classified as group D in eight cases and group B in one case. Six of the seven patients who had cancers too extensive for control had lesions classified as group D and one as group C.

While patients with larger squamous cell carcinomas have a distinctly poorer prognosis, it is not to be inferred that large size, in itself is a contraindicatory factor as far as chemosurgery is concerned. A considerable number of patients who were incurable by ordinary surgical or radiation treatment were successfully treated by the chemosurgical method because of the facility with which the ramifying radicles of the advanced carcinoma could be followed out.

The effect of previous treatment on prognosis is considerable. This is indicated by the five-year cure rate of only 68 1 per cent in the group of 114 patients who received previous surgical or radiation treatment as compared to the rate of 93 per cent in the group of 242 patients who had not received previous treatment.

The adverse effect of previous treatment with roentgen rays, radium or surgery on prognosis was largely because of the delay occasioned by the use of these procedures. This delay in turn, allowed the neoplasm to become large and then

to metastasize, invade vital structures or become so extensive that complete eradication was not feasible. Moreover, in some cases there was evidence that the cancer had been scattered by the surgical procedures while in other cases the barriers to spread through fascial planes and other cleavage planes were broken down In some cases in which the patients had been treated extensively with roentgen rays or radium there was evidence of an increase in the degree of malignancy and occasionally these treatments seemed to increase the tendency to spread widely in special structures such as the nerve sheaths or the dermis.

The rate of cure of 68 1 per cent for the group of patients with recurrent cancer indicates that the chemosurgical method makes possible the salvage of a considerable number of patients who otherwise would not be cured. Indeed the most definite indication for chemosurgical treatment often is the lesion which has resisted other forms of therapy

Previously treated lesions may be somewhat more difficult to remove chemosurgically than lesions which have not been treated before because the scar from the radiation or surgery may tend to obscure the gross outlines of the neoplasm. For this reason in cases of recurrent cancer it often is necessary to omit or to reduce the scope of the initial surgical excision of the main mass and to rely on the microscopically controlled chemosurgical excisions throughout.

The effect of the histologic grade of malignancy on prognosis is profound. This is indicated by the drop in the rate of cure from 97 0 per cent in the group with Broders grade 1 squamous cell carcinomas to 33.3 per cent in the group with grade 4 lesions (Table XXXVI) Fortunately highly malignant cutaneous carcinoma is less common than those of lower malignancy this is apparent from the distribution of cases in the four grades of malignancy as follows grade 1, 28 4 per cent of the cases grade 2 43.5 per cent grade 3 22 2 per cent and grade 4 5 9 per cent.

TABLE XXXVI

EFFECT OF HISTOLOGIC GRADE OF MALIGNANCY OF SQUAMOUS CELL CARCINOMA OF THE SKIN ON FIVE YEAR END RESULTS

Grade	Number of Lesions	Successful Results Number	Per cent
1	101	98	97 0
2	155	143	92 3
3	79	54	68 3
4	21	7	33 3

Much of the adverse effect of increased malignancy was because of the associated higher incidence of metastasis. This was reflected in the group of patients with metastases by a shift toward the higher grades of malignancy as follows grade 1 2 7 per cent grade 2 29 7 per cent grade 3 43 3 per cent and grade 4 24.3 per cent. However much of the adverse effect of high malignancy was also because of a greater tendency for deep invasion into underlying vital structures. In the group of cases with such deep invasion there was a similar shift in the distribution toward higher malignancy

In the absence of metastasis or invasion of vital structures, the chemosurgical method is as effective in highly malignant carcinoma as it is in carcinoma of lower malignancy Actually the patient with the highly malignant, infiltrating carcinoma may be in the most dire need of the rapid sure eradication made possible by the chemosurgical technic.

The effect of the site of origin on prognosis in cases of squamous cell carcinoma of the skin is not particularly notable (Table XXXVII)

TABLE XXXVII

EFFECT OF SITE OF ORIGIN OF SQUAMOUS CELL CARCINOMA OF THE SKIN ON FIVE-YEAR END RESULTS

Site	Number of Lesions	Successful Results Number	Per cent
Face and head	164	139	84 8
Nose	43	37	86 4
Ear	54	43	79 6
Eyelid	14	13	92 9
Extremities and trunk	81	70	86 4
All sites	356	302	84 8

Thus, the cure rate was highest for patients with carcinoma of the eyelid (92.9 per cent) and lowest for carcinoma of the ear (79 6 per cent) The relatively lower rate for the latter group was explainable by the closeness of the ear to underlying vital structures and to large

lymphatic vessels through which metastasis could take place more readily On the other hand the eyelid is not so near to vital structures and there is much less tendency for metastasis to occur through the relatively smaller lymphatic vessels.

The effect of metastasis on prognosis is most serious as indicated by the fact that in the group of forty four patients with metastasis, successful five year end results were obtained in only three (6.8 per cent) By way of contrast in the group of 312 patients without metastasis successful results were attained in 299 cases (95 8 per cent)

Further evidence of the seriousness of metastasis as a complication of carcinoma of the skin was the fact that forty four of the fifty four unsuccessfully treated patients had metastases.

In twenty two cases resection of the metastatic nodes was carried out by various members of the surgical staff but in only three cases were successful five year end results obtained. No prophylactic resections of non palpable regional nodes were carried out, but this does not mean that this procedure might not be indicated in selected cases in which metastasis to accessible nodes would seem likely because of the large size and high grade of malignancy exhibited by the primary lesion. In two cases enlarged nodes were resected but no carcinoma was present. In a number of patients the nodes were resected purely for palliative purposes. In several patients who had inoperable metastatic nodes, palliative roentgen therapy was employed.

Several patients whose cases are included in this series had inoperable regional metastases but the primary lesion was chemosurgically removed for the purpose of palliation.

Comparison of Results with Those of Other Authors

The unprecedented reliability of the chemosurgical method in the treatment of carcinoma of the skin is indicated by comparison with the statistical results from other centers for cancer treatment. One of the best series, with respect to both statistical validity and also excellent therapeutic results is that of Magnussen[41] who reported on the results obtained in a series of 1,343 cases of patients treated with the highly developed radiologic, surgical and electro-surgical techniques employed at Radiumhemmet and associated Institutions in Stockholm, Sweden. From his protocols it was determined that the five year rate of cure in his series of 363 determinate cases of carcinoma of the skin was 82.6 per cent. In the present series of 1,554 cases of cutaneous carcinoma there were 1,138 cases in the determinate group and the five year cure rate was 94 0 per cent. The two series were made up of cases which were essentially similar in the Radiumhemmet series the lesions were in the larger size groups (C and D) in a somewhat higher proportion of the cases (36.2 per cent as compared to 27.2 per cent in the present series) but his series contained fewer recurrent lesions (27 8 per cent as compared to 33.5 per cent in the present series) and fewer squamous cell carcinomas (23 9 per cent as compared to 31 1 per cent in the present series)

The above statistics from the Radiumhemmet are not the latest from that institution but they were used because of the lack of detail in the current reports. However the latest report[77] on the five year end results for the patients treated from 1921 through 1947 yielded the following approximate data There were 6,128 cases of cancer of the skin of which 3 104 were indeterminate and 3 024 determinate. In the latter group there were 376 cases in which the patients were unsuccessfully treated and 2,648 in which they were successfully treated. The five year rate of cure therefore was 87 6 per cent. The rate of 94 0 per cent attained by means of chemosurgical treatment surpasses these results.

Another comparable and statistically adequate series is that reported by Warren, Simmons and Rea[103] from Huntington Hospital in Boston for a group of 829 patients of whom 84 0 per cent were traced they reported a five year cure rate of 76 0 per cent. Some excellent results have been reported in the treatment of cancers falling in the realm of dermatology However such series are composed for the most part, of patients with relatively small lesions, whereas the present series includes the cases of a large number of patients whom the dermatologist ordinarily would refer to a sur

geon and it even includes an appreciable number of patients whose cancers ordinarily would be considered inoperable

Because of the poorer prognosis associated with squamous cell carcinoma as compared with basal cell carcinoma the therapeutic results in a given series of cutaneous carcinoma are strongly affected by the proportions of the two types of neoplasms. Hence, more accurate comparison with other series may be accomplished by separate consideration of basal and squamous cell carcinomas.

In Magnussen's series of 272 determinate cases of basal cell carcinoma the five year cure rate was 88.2 per cent as compared to 98 2 per cent in the present series of 782 determinate cases in which the patients were treated by means of chemosurgery Similarly in the group of ninty-one cases of squamous cell carcinoma reported by Magnussen the five year cure rate was 65 9 per cent as compared to 84 8 per cent in the present series of 356 determinate cases in which the patients were treated chemosurgically

Advantages of Chemosurgical Treatment

In the treatment of cancer of the skin the chemosurgical method has several advantages of which the chief are (1) reliability (2) conservatism, and (3) low operative mortality

The reliability of the chemosurgical method has been documented in the preceding chapters by numerous photographs of patients with cancer of the various areas of the skin and by the foregoing statistical analysis of the therapeutic results. The statistics were highly valid because only 2.1 per cent of the patients were lost from observation, while ordinarily the data on a series of this sort is considered valid if no more than 10 per cent of the patients are lost track of The therapeutic results excel the best reported results in comparable series in which the patients were treated by means of the usual surgical and radiologic technics. This record was attained despite the fact that the present series included not only the general run of patients from Wisconsin and adjacent states but also a considerable number of patients who had not responded to the measures available in other sections of the country In general, the only circumstances which prevented favorable results were invasion of vital structures or uncontrollable metastasis. In the groups of patients with squamous cell carcinoma the development of metastasis following chemosurgical treatment was infrequent This observation bore out results of the animal experiments which indicated that chemical treatment had no tendency to increase metastatic spread.

The second major advantage of chemosurgery in the treatment of cancer of the skin is the conservatism. This is due to the microscopic control which makes it unnecessary to remove wide swaths of normal tissue in order to be reasonably sure of the eradication of the cancer The conservation of maximal amounts of uninvolved tissue coupled with the excellent conditions for healing following chemosurgical treatment makes a repair unnecessary in a great majority of the cases. In those in which the cancer has invaded so widely that a defect requiring a repair has been produced the preservation of maximal amounts of normal tissues facilitates satisfactory reconstruction

Both the reliability and the conservatism of the chemosurgical method are due to the systematic microscopic control of excision which makes it possible to selectively follow out the unexpected extensions from the main mass of the cancer These "silent" extensions are much more common in cutaneous carcinoma than was ever appreciated before the advent of chemosurgery The various patterns of spread exhibited by these outgrowths are considered in detail in Chapter 21

The third major advantage of the chemosurgical method for the treatment of cancer of the skin is the low operative mortality rate. Despite the unusually large proportion of patients with extensive cancers in the present series of 1,554 cases of carcinoma of the skin there were only five deaths during or shortly after chemosurgical treatment. Thus, the mortality rate was 0 32 per cent. Two patients died while under treatment for carcinoma which invaded the brain, one in the temporal region and one in the ethmoid area. Two patients died of coronary thrombosis one during treatment and the other four days after completion of treatment. The fifth patient died of throm-

bosis in the internal carotid artery following ligation of the external carotid artery. The low mortality rate is largely attributable to the lack of need for a general anesthetic. This is an important consideration in view of the fact that many patients with cutaneous cancer are elderly and in poor general health.

The chemosurgical method also has certain technical advantages which extend operability to a considerable group of patients with cancers which ordinarily would be considered inoperable because of extensiveness, difficult position or other factors. Some of the photographs of patients illustrate this point. Not a few surgeons and especially plastic surgeons,[71] feel that it is advisable to refer patients for chemosurgical removal of extensive or troublesome cancers. Then, since there is considerable assurance that the cancer has been eradicated they can concentrate on any necessary reconstruction without fear of disseminating the neoplasm.

In contrast to radiation therapy, there is no danger of late sequelae such as atrophy, ulceration or carcinoma. Any tissue damaged by the fixative chemical is removed promptly and hence it can cause no subsequent complications. Moreover, the scars from chemosurgical treatment, in contrast to burn scars or radiation scars, never break down or proceed to develop cancer.

Chemosurgical excision has no tendency to scatter neoplastic cells. Furthermore, if some of the cancer is missed, the residual foci promptly make their presence known because they are not imbedded deeply in a surgical scar nor are they held in check for an indefinite time in an indurated scar such as may follow radiation therapy.

In the treatment of carcinoma of the skin these advantageous features more than counterbalance the disadvantageous features of the chemosurgical technic. Among the latter may be mentioned the necessity of learning the specialized technic, the need for a specially trained technician to prepare the frozen sections, the time consuming process if the neoplasm extends considerably farther than expected and the discomfort to the patient if the lesion proves to be extensive. The last two disadvantages seem inconsequential when it is considered that many patients with such extensive cancers would have relatively little chance of obtaining a cure by any other method.

Comment

Although this book chiefly concerns the treatment of cancer which already has developed, there should be no lack of emphasis on means of prevention. Since some squamous cell carcinomas are produced by the action of ultraviolet rays it is obvious that the avoidance of overexposure to sunlight is to be recommended in individuals who sunburn readily. This preventive measure is more fully discussed in Chapter 27 along with methods for the removal of precancerous lesions.

Detailed description of the numerous variations in the histopathology of the various cutaneous neoplasms is omitted here because this subject has been well covered in many articles in the literature of dermatology and pathology as well as in books such as those of Lever,[43] Ormsby and Montgomery,[72] Andrews,[8] Eller and Eller,[29] Allen,[3] and McKee and Cipollaro.[64] As regards basal cell carcinoma, it is convenient to indicate the various clinical types by terms such as nodulo-ulcerative (including nodular and rodent ulcer types), pigmented, morphea like and superficial, while histopathologically basal cell carcinoma is classified into two groups, undifferentiated (including solid, pigmented, morphea like or superficial types) and differentiated (including cystic, adenoid and keratotic types).[43] However, in order to indicate the clinical behavior of a lesion the simplest and most significant classification is according to the degree of invasiveness (high invasiveness or low invasiveness); hence, the latter classification has been used in the sections on the therapeutic results. Similarly squamous cell carcinoma may be given various descriptive terms but the most meaningful classification is that of Broders by which the neoplasms are placed in four grades according to their degree of malignancy as indicated by the amount of keratinization, pleomorphism, nuclear hyperchromasia and the number of mitoses.

Needless to say anyone contemplating the use of the chemosurgical method not only should be

thoroughly familiar with the clinical and histologic appearance of the different types of malignant neoplasms but they also should be able to recognize the various benign tumors and the many dermatologic conditions which may simulate some of the features of cancer. Examples of the latter category include such diverse skin diseases as lichen planus, psoriasis, granuloma annulare, chronic radiodermatitis, pyoderma gangrenosum, lupus vulgaris and other forms of cutaneous tuberculosis, bromoderma, sarcoid, leprosy, anthrax, syphilis, blastomycosis, actinomycosis, molluscum contagiosum, verruca vulgaris, chronic discoid lupus erythematosus, pseudoepitheliomatous hyperplasia and many others. Benign tumors and precancerous lesions which must be differentiated from cutaneous cancer also include a considerable variety of conditions including the following: nevus verrucosus, nevus sebaceus, senile sebaceous nevus, sebaceous adenoma, epidermal and sebaceous cysts, senile keratosis, cutaneous horn, seborrheic keratosis, syringocystadenoma papilliferum, syringoma, mixed tumor, cylindroma, trichoepithelioma and calcifying epithelioma as well as nevocellular nevi and tumors arising from the underlying fibrous tissues.

CHAPTER 9

Carcinoma of the Lips

IN the treatment of carcinoma of the lips the chemosurgical method has three advantages (1) unprecedented reliability (2) maximal conservatism with correspondingly good cosmetic results, and (3) low operative mortality[44] The first two advantages result from the microscopic control of excision which makes it possible to accurately follow out and eradicate the "silent extensions from the main neoplastic mass the third advantage results largely from the lack of need for a general anesthetic.

Technic

Although previously described and illustrated (Chapter 2 Fig 1) the chemosurgical technic is redescribed herewith in order to emphasize certain details of the procedure as it is used in the treatment of carcinoma of the lips.

Ordinarily the main mass of the cancer is surgically excised under local anesthesia. In preparation for the excision of carcinoma of the lower lip or the commissures procaine hydrochloride in a 1.5 per cent solution is injected around the mental nerve at its exit from the mental foramen and then into the lip to form a wall of anesthesia around the cancer Care is exercised to avoid injection into the immediate vicinity of the neoplasm not only because of the possibility of implantation of cancer cells along the needle tract but also because the injected solution may interfere with the action of the fixative chemical.

The initial excision usually is done with a scalpel. With experience, the operator learns to accurately follow along the under surface of the main mass of the cancer A curet occasionally is useful to remove pockets of malignant tissue but as a rule it is unnecessary During excision partial hemostasis may be accomplished by having an assistant hold the lip between the thumb and finger The pressure is maintined while dichloracetic acid is quickly applied to cauterize the surface and stop the capillary bleeding Arterial bleeding often requires the application of a square of fixative impregnated gauze under pressure for a few minutes. If after cauterization of the surface an area of residual carcinoma is seen grossly another layer of tissue may be excised and the area again cauterized. Then dichloracetic acid is applied to a millimeter or so of skin and mucosa at the periphery and the zinc chloride fixative paste is applied in a thickness sufficient to enable the removal of a layer 1 to 2 mm. thick at the next visit. The cotton dressing and the overlapping petrolatum-spread cotton dressing are then affixed with quarter inch waterproof adhesive tapes which are placed to follow the contour of the lip (Fig 112B) If the lesion extends for a considerable distance into the mucosal side of the lip it is necessary to place half inch tapes in an anterior-posterior direction the posterior ends will not stick to the mucosa, of course but they will be held in place by the pressure between the lip and the teeth. Dressings at the corner of the mouth also are retained by half inch tapes which are held in place by the pressure between the cheek and the teeth. Dressings for the upper lip are similar to those for the lower lip Special care is exercised to make the mucosal side of the dressing watertight petrolatum may be applied to the posterior part of the completed dressing to help to accomplish this. The patient is cautioned to use care in eating and drinking so as not to disturb or wet the dressing. To do this it may be necessary for him to take his fluids from a

spoon. Most patients are treated on an out patient basis and many go about their business as usual. An analgesic such as codeine ½ grain (30 mg.) and aspirin 10 grains (0.6 gm.) or an equivalent proprietory preparation such as "Codempiral no 3" ordinarily is prescribed for use every three hours as needed

The next layer of tissue may be excised after a period of from one to forty-eight hours depending on circumstances. The incision is made through fixed tissue so there is no pain or bleeding from this operation. As the layer is excised for microscopic examination, the origin of each of the specimens is indicated by making marks with mercurochrome on the whitish fixed tissue (Fig 112C). A corresponding map is drawn on a pad of paper. The frozen sections which are made by cutting through the under surface of the flat specimens are examined systematically and the areas of cancer marked on the maps with a red pencil (Fig 112D). Reapplication of the fixative is limited to the cancerous areas and further excisions are made as indicated by the presence of microscopically located cancer. At the completion of treatment a thin layer of fixed tissue remains (Fig 112E). This either is covered with a petrolatum gauze dressing or as usually is the case petrolatum is applied and the lesion left uncovered. If the labial artery has been approached or cut and the pressure in the vessel seems high enough to cause some possibility of bleeding as the fixed tissue loosens, it is advisable to insert suture-ligatures around the vessel. This is done by passing the needle through the fixed tissue after the area has been infiltrated with procaine. Often a small piece of oxidized cellulose (oxycel cotton) is supplied to the patient to hold on the lesion if bleeding should occur

The final layer of fixed tissue may be allowed

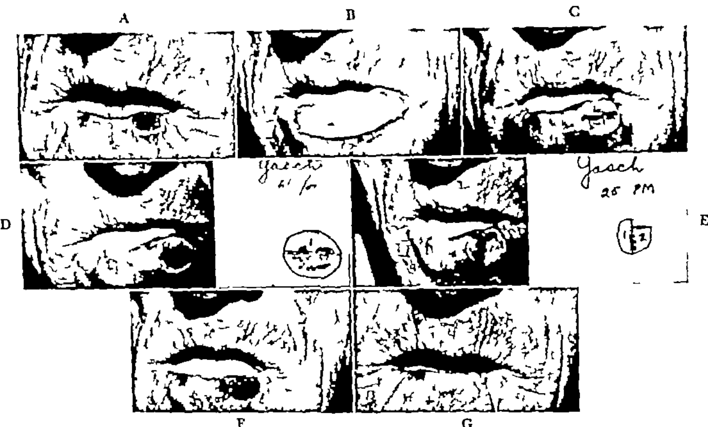


Fig 112. (A) Squamous cell carcinoma, grade 2 malignancy (B) Dressing to hold fixative in place. (C) Fixed tissue after excision of a layer of tissue for microscopic examination. The transverse mark was made with mercurochrome to show the origin of the two specimens. (D) Reapplication of the fixative to the area of cancer the location of which is indicated by the shading on the map to the right. (E) Lesion after excision of another layer after three hours. As indicated on the map to the right there was no cancer at this level (F) Granulation tissue after separation of the final layer of fixed tissue three days later (G) Healed lesion. There was no recurrence after five years.

to separate spontaneously if the lesion is small but if large it is advisable to have the patient return in about four days so that the slough may be removed with a sharp-pointed scissors (Fig 112F) After removal of the fixed tissue the lesion either may be covered with a scarlet red ointment impregnated gauze dressing or as usually is the case mercurochrome may be applied and the wound left uncovered. The granulation tissue is remarkably healthy and larged nodes are occasionally recommended if the primary carcinoma is large (2 or 3 cm. or more) and the grade of malignancy is high (high grade 2 or higher)

The patient is observed at intervals of one to three months for the first year the interval depending upon the likelihood of recurrence or metastasis in the individual case After that the patient is seen every three to six months until five years have elapsed. The patient is cautioned



Fig 113 (A) Squamous cell carcinoma, grade 2, which the patient stated was recurrent after V-excision and roentgen therapy two years previously However there was a possibility that this represented a new primary lesion. (B) Granulation tissue after chemosurgical excision. The carcinoma extended posteriorly in the submucosa for 8 to 10 mm. beyond the clinically apparent edge of the carcinoma. (C) Healed lesion. There was no recurrence after ten years.

germ-resistant. Most lesions heal in a week or so and the resulting scars usually are virtually invisible (Fig 112G)

If regional nodes are palpably enlarged and the consistency and fixation are suggestive of metastatic involvement an immediate neck dissection is indicated. If there is definite involvement of the submental and submaxillary nodes a radical neck dissection with removal of the sternocleido-mastoid muscle and the jugular vein is indicated. If the enlarged nodes are thought to be inflammatory they may be observed for two or three weeks, but if there is any doubt after that interval, the neck dissection should not be delayed. Prophylactic neck dissections in the absence of palpably en to return immediately if he notices any evidence of recurrence or metastasis.

Virtually all carcinomas arising on the vermilion border of the lips are of the squamous cell type. The lower lip is involved much more commonly than the upper lip Those affecting the commissures practically always arise either on the adjacent lower or upper lip and hence no separate classification is made for commissural lesions in the section on therapeutic results.

Lower Lip

The microscopic control of excision which characterizes the chemosurgical technic makes it safe to remove carcinomas of the lip at a

very conservative level As a consequence the cosmetic results are unusually good The mucosal epithelium covers the scar and makes it virtually invisible unless the lip is blanched usually is less noticeable than the scar of a V-excision (Fig 113) When the orbicularis oris muscle is appreciably involved some degree of defect may result (Fig 114) However such



Fig 114 (A) Squamous cell carcinoma, malignancy grade 2. The entire right half of the lip was affected. (B) Granulation tissue after chemosurgical excision of the carcinoma which invaded for a centimeter into the orbicularis oris muscle. Metastatic regional nodes were dissected surgically by Dr F G Hidde. (C) Healed lesion with minimal defect. There was no recurrence after fifteen years.



Fig 115 (A) Squamous cell carcinoma, grade 2 malignancy (B) Granulation tissue and definite defect which followed chemosurgical removal of the deeply invasive neoplasm. The patient refused a repair (C) Healed lesion after six years. The defect had flattened out forming a lip that was functionally and cosmetically satisfactory

by digital pressure Following the removal of small and medium-sized cancers it often is difficult to see where the lesion had been (Figs. 1 and 112) Even after the removal of somewhat larger lesions the resultant scar defects tend to correct themselves in the course of several months (Fig 115) Only after the removal of very deep-seated lesions does there result a niche which requires a repair Some carcinomas affect a large area of the surface of

A B C

D

Fig 116 (A) Squamous cell carcinoma, grade 2 malignancy (B) Everted lip to show extent of invasion into the mucosa. (C) Granulation tissue after chemosurgical excision. (D) Healed lesion. There was no recurrence after five years.

A B C

D

Fig 117 (A) Squamous cell carcinoma, grade 1 malignancy The lesion had recurred after radium irradiation and operation. (B) Granulation tissue after chemosurgical excision. (C) Healed lesion. There was insufficient structure for good function, so an immediate repair was carried out. (D) Condition four months later A neck dissection was done but no metastatic nodes were found.

the lip without appreciably invading its deeper structures these neoplasms may be chemosurgically removed so conservatively that the final cosmetic and functional result is quite satisfactory (Fig 116)

In cases in which so much of the lip has been removed that there is difficulty in eating and drinking an immediate repair is indicated. Since there usually is plenty of healthy tissue obtainable from the adjacent cheeks and chin, a satisfactory repair may readily be accomplished (Fig 117)

Upper Lip

Carcinoma arising on the upper lip proper is almost always squamous cell in type the rare basal cell carcinoma of the upper lip is usually found on close scrutiny, to have arisen on the skin just above the vermilion border (see Chapter 3) The conservative removal which is possible with the chemosurgical technic results in unusually good cosmetic results (Fig 118)



Fig 118. (A) Squamous cell carcinoma, grade 1 malignancy (B) Healed lesion after chemosurgical excision. There was no recurrence after five years.

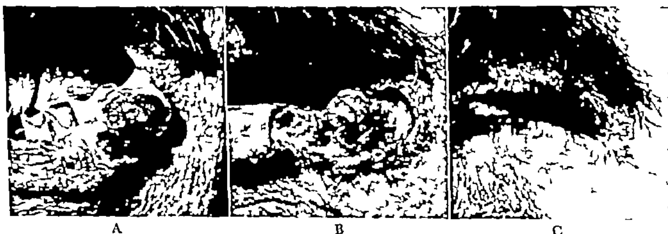


Fig 119 (A) Squamous cell carcinoma, grade 2 malignancy (B) Granulation tissue after chemosurgical excision. (C) Healed lesion. There was no recurrence after fourteen years.

Commissures

Most commissural lesions clearly have originated on either the lower lip (Fig 119) or upper lip Most authors report poorer results in the treatment of cancer at the angles of the mouth probably because of increased technical difficulties. However with the microscopically controlled chemosurgical technic the

prognosis is virtually the same as elsewhere on the lips For that reason in analyzing the thera peutic results the commissural lesions have been placed in the lower lip and upper lip categories according to the predominant site of origin.

Therapeutic Results in Cases of Squamous Cell Carcinoma of the Lips

Altogether 326 squamous cell carcinomas were removed from the lips by means of the chemosurgical technic during the twelve year period which ended six years prior to this writing The cancers were in all stages from early to ad vanced Those which affected the upper lip and commissures were included along with the more common carcinoma of the lower lip Previous unsuccessful surgical or radiologic treatment had been received by 20.7 per cent of the patients. Metastasis was present in 10.5 per cent of the patients but a definite diagnosis of metastasis at the initial examination was made in only 5.3 per cent.

The 326 cases were divided into "indeter minate" and determinate" groups. The in determinate group included the cases of fifty three patients who had no recurrence when they died of other causes before the elapse of five years and the cases of seven patients who

TABLE XXXVIII
FIVE-YEAR END RESULTS FOR SQUAMOUS CELL CARCINOMA OF THE LIPS

This series includes the cases of all patients with histologically proved squamous cell carcinoma, both early and advanced, previously untreated and recurrent, with and without metastasis, who were chemosurgically treated during the twelve year period ending six years prior to this writing

Total number of cases	326
Indeterminate group total number	60
Patients dead from other causes without recurrence	53
Patients lost from observation without recurrence	7
Determinate group, total number	266
Unsuccessful results, total number	22
Patients dead, cancer present at death	15
Patients lost from observation with cancer	6
Patients living with cancer	1
Successful results, patients free from cancer for five years or more	244
Five-year rate of cure (244 + 266) × 100	91 7%

had no cancer when they were lost servation before the end of the five ye The determinate group was compos twenty two cases in which treatment successful and the 244 cases in which was successful (Table XXXVIII)

Therefore the five year cure rate cinoma of the lips was 244 — 266 or cent.

The effect of the size of the lesion nons is considerable as indicated by crepancy between the cure rate of 98.4 in the group of cancers under 1 cm. cure rate of 47 1 per cent in the cancers over 3 cm. in average diamete XXXIX) Examples of lesions in th

TABLE XXXIX
EFFECT OF SIZE OF SQUAMOUS CARCINOMA OF THE LIPS O FIVE-YEAR END RESULTS

Group	Average Diameter Cm	Number of Lesions	Success Number
A	under 1	64	63
B	1 to 2	140	134
C	2 to 3	45	39
D	3 or more	17	8

groups according to size are given illustrations as follows group B diameter 1 to 2 cm.) in Figures 112, 119 group C (2 to 3 cm.) in Figure and 116 and group D (over 3 cm.) in 113 and 115 The adverse effect of l was attributable mainly to the fact large neoplasm had more opportu metastasize. Thus, the cause of fa seventeen of the twenty two unsuc treated cases was metastasis which c be controlled. However in three c neoplasms were so extensive that tl plete eradication of the primary les not feasible in two of these cases plasm had extensively invaded the n through the inferior dental canal whil third case the advanced neoplasm eradicated because of the non-cooperat demented patient. One patient was co to have been unsuccessfully treated bec died of a coronary occlusion during surgical treatment of the medium-si cinoma of the upper lip.

The effect of previous treatment on prognosis is considerable as indicated by the cure rate of 83 6 per cent in the group of fifty five patients who received previous treatment as compared to the rate of 93 8 per cent in the group of 211 patients who had received no previous treatment. The greater proportion of failures in the group of patients who had received previous treatment was largely attributable to the delay occasioned by the ineffectual treatment. This delay allowed the neoplasms to become sufficiently advanced to metastasize or to spread so widely that complete removal was not feasible.

The effect of the histologic grade of malignancy on the prognosis of squamous cell carcinoma of the upper and lower lips is profound as indicated by the drop in the five-year cure rate from 98.5 per cent for grade 1 lesions to 28 6 per cent for grade 4 carcinomas (Table XL) The chief reason for the adverse influence of high malignancy on prognosis was the greater incidence of associated metastasis.

TABLE XL

EFFECT OF HISTOLOGIC GRADE OF MALIGNANCY OF SQUAMOUS CELL CARCINOMA OF THE LIPS ON FIVE-YEAR END RESULTS

Grade	*Number of Lesions*	*Successful Results Number*	*Per cent*
1	67	66	98 5
2	157	147	93 6
3	35	29	82 8
4	7	2	28 6

The effect of site of origin on prognosis is appreciable in that the rate of cure is less for carcinoma of the upper lip than for carcinoma of the lower lip Thus, in the group of 309 cases of squamous cell carcinoma of the lower lip there were 251 determinate cases with 232 five-year cures giving a five-year cure rate of 92 4 per cent. In the smaller group of seventeen cases of squamous cell carcinoma of the upper lip there were fifteen determinate cases and of these twelve were successfully treated yielding a five year cure rate of 80 per cent. This difference is an expression of the tendency toward lower malignancy in carcinomas of the lower lip where the exogenous carcinogenic factors of smoking and exposure to sunlight and wind are more strongly operative.

The effect of metastasis on prognosis is great as indicated by the fact that only eleven of twenty eight patients with metastasis were cured (39.3 per cent) while 233 of 238 patients without metastasis had a successful outcome (97 9 per cent) In the group of fourteen cases in which a definite diagnosis of regional metastasis was made at the initial examination there was a five year cure rate of 50 0 per cent while in the group of 252 cases in which metastasis was not initially diagnosed the cure rate was 94 0 per cent.

Although most metastatic nodes were resected by standard surgical methods by Dr E. R. Schmidt and his staff[34] some firmly fixed submaxillary masses were chemosurgically excised. While most of these chemosurgical excisions were for the purpose of removing large ulcerated malodorus, inoperable masses for temporary palliation, some of the patients apparently were cured (Fig 120) In patients in whom chemosurgical removal of the large submaxillary mass proves feasible, a surgical dissection of the cervical nodes should follow

Comments

The certainty with which the primary carcinoma of the lip may be eradicated by the chemosurgical method is indicated by the fact that in this series of 326 cases there were only four cases in which unsuccessful treatment could be attributed to failure to eradicate the primary lesion. In two of these cases the cancer invaded the mandible so extensively that complete removal was not practical in one case treatment was incomplete because of the noncooperation of a demented patient and in one case the patient died of a coronary occlusion before the completion of treatment. Thus, it is apparent that in the absence of extenuating circumstances the primary lesion may be eradicated in virtually every case and it is the occurrence of uncontrollable metastasis that accounts for most of the failures.

The five-year cure rate of 91 7 per cent surpasses the results reported by other workers (Table XLI) However it is only fair to point out that in some centers a larger proportion of advanced and recurrent lesions are seen. For example in the series reported by Martin Mc



A B C

Fig 120 (A) Fixed submaxillary nodes secondary to squamous cell carcinoma of the lower lip (the latter had been treated elsewhere with radon seeds over a period of two years after which a surgical resection and plastic repair were done. (B) Granulation tissue after chemosurgical excision. The mandible, and the sternocleidomastoid and mylohyoid muscles are shown exposed. The cancer had invaded the submaxillary salivary gland and the periosteum of the mandible (C) Healed lesion. There was no recurrence when the patient was examined one year later he died of undetermined cause after three years.

Comb and Blady[47] and in the series of Ward and Henrick,[103] there were more cases with metastases, more with large primary lesions and more with recurrent cancers than in the present series. However this is not to indicate that patients with far advanced cancers were not admitted to the present series. On the contrary a considerable number of patients with cancers which ordinarily would be considered inoperable were accepted for chemosurgical treatment. Apparently however the proportion of patients whose cancers were recognized and brought to treatment at an early stage was somewhat greater in this than in some other reported series. Over the years there has been a noticeable trend toward earlier diagnosis and more prompt treatment as a result of educational campaigns directed to both laymen and physicians. Reflecting this improvement is a steady rise in the rate of cure. Thus, ten years ago the five year

TABLE XLI

COMPARISON OF THE FIVE-YEAR END RESULTS OF CHEMOSURGICAL TREATMENT OF CARCINOMA OF THE LIP WITH THE END RESULTS OF OTHER AUTHORS

		Metastases		*Size of Primary Lesion*		*Previously Treated*	*Five-Year End Results*		
Author	*Treatment*	*Present Sometime Per cent*	*Present On Admission Per cent*	*Small A & B Per cent*	*Large C & D Per cent*	*Per cent*	*Total Cases*	*Determinate Cases*	*Cure Rate Per cent*
Mohs	Chemosurgery	10.5	5.3	76.7	23.3	20.7	328	266	91.7
Martin *et al* [47]	Surgery and radiation	34.2	27.8	57.0	43.0	27.1	375	315	70.0
Ward and Henrick[103]	Surgery and radiation	23.3	?	60.3	39.7	30.5	259		70.1
Schreiner and Christy[85]	Radiation	?	?	?	?	?	636	504	74.4
Bergendal[13]	Radium	?	?	?	?	?	172	137	80.3
Newell[71]	Surgery	?		?	?	?	328	294	61.6

cure rate attained with the chemosurgical method was 87.5 per cent[44] whereas it now is 91 7 per cent

The microscopic control of excision provided by the chemosurgical technic not only makes possible the more reliable destruction of the cancer but it also makes it safe to practice conservatism. The great majority of cancers can be removed chemosurgically without noticeable scar or deformity Of course more advanced lesions necessitate the destruction of larger amounts of labial tissues and the resultant defects require repair but even then the preservation of maximal amounts of healthy tissue greatly facilitates a satisfactory reconstruction

The importance of the microscopic guidance afforded by the chemosurgical technic was demonstrated repeatedly during the removal of carcinomas of the lips Often thin sheets or slender strands of cancer cells were followed for some distance beyond the clinically detectable mass. Frequently the orbicularis oris muscle exhibited somewhat greater resistance to the spread of the cancer that did the tissues just anterior and posterior to this structure. However some cancers readily pushed their way in between the muscle fibers indicating that the muscle is a barrier to some but not to all cancers. Some cancers had a particular affinity for the submucosa therefore most of their "silent" spread was under the apparently normal mucosa posterior to or to the sides of the mass. In a few instances the cancer exhibited a strong affinity for the dermis of the adjacent skin. In two instances the cancer extended in the dermis as a thin sheet which almost reached the chin In many cases in which there was an almost imperceptible blending of the carcinoma with the keratoses and areas of leukoplakia on the adjacent mucosa the microscopic guidance was invaluable in determining just how far the carcinoma extended. Often the neoplastic change extended for an unexpectedly great distance under the hyperkeratotic mucosa.

Some degree of selective affinity for nerve sheaths has been demonstrated microscopically in fourteen of the 666 cases of carcinoma of the lip observed to date an incidence of 2.1 per cent (Fig. 163) In several cases the cancer followed the mental nerve through the mental foramen and extended for several centimeters along the inferior dental canal One metastatic mass in the submaxillary region and the posterior cheek extended for several centimeters in the perineurium of the buccinator and facial nerves the cancer in the latter structure was followed into the stylomastoid foramen and this precluded any hope of a cure

There are other advantages to chemosurgical treatment besides the reliability and conservatism. For example the mortality rate in this series was extremely low only two patients died during chemosurgical excision. One died of sepsis from a massive cervical metastatic mass while an attempt was being made to remove the primary mass on the lower cheek and mandible as a palliative measure the other died of a coronary occlusion before the removal of an upper lip lesion had been completed. Therefore the operative mortality rate was 0 6 per cent. The rate for carcinoma of the lower lip was 0.3 per cent for carcinoma of the upper lip 5.9 per cent. Much of the low operative mortality rate may be attributed to the fact that no general anesthetic is used during chemosurgical treatment. This factor alone is important inasmuch as many of the elderly patients with carcinoma of the lip are not good operative risks.

Another factor that contributes to the low risk during chemosurgical treatment is the lack of complicating infection this is in spite of the high incidence of oral sepsis in patients with carcinoma of the lips. During the period of active treatment the fixative chemical sterilizes the treated area, and by the time the final layer of fixed tissue is ready to separate a highly infection resistant granulation tissue has formed. What surface infection there is does no harm and epithelization invariably progresses rapidly to completion.

No complications develop in the scars after healing regardless of the size of the defect. There is none of the atrophy ulceration or necrosis such as may follow intensive radiation therapy If the carcinoma involves the mandible or maxilla the involved bone is cleanly removed and there is no danger of osteonecrosis or osteomyelitis.

A factor of some economic importance is the fact that the great majority of patients with cancer of the lip may be chemosurgically treated without being hospitalized. In fact, many patients go about their business with only a few hours loss of time.

Precancerous and Benign Lesions

A number of precancerous and benign lesions must be distinguished from carcinoma of the lip Among the precancerous lesions may be mentioned keratoses squamous cell papilloma, chronic ulcers and fissures, radiation ulcers and leukoplakia. The most common benign neoplasm of the lip is hemangioma but occasionally other benign lesions are encountered, as for example granuloma pyogenicum, mucinous and sebaceous cysts, melanosis, sarcoid, nevi, fibroma and discoid lupus erythematosis. These conditions are considered in later chapters.

CHAPTER 10

Carcinoma of the Mouth

THE use of the chemosurgical method in the treatment of intraoral neoplasms is limited by the tendency for the saliva to dilute the fixative chemical. However this diluting effect can be overcome if the lesions are on the hard palate or upper alveolar ridge because the patient's dentures or a temporary plate may be used to hold the fixative and the dressings in place. Cheek lesions also can be treated chemosurgically with the dressings being held in place by adhesive tapes affixed to the skin on the outside of the cheek and placed so that they are held in place by pressure between the cheek and the teeth on the inside of the mouth (Fig 121) Lesions in the floor of the mouth, on the tongue and in the faucial regions often are treated more readily by electrosurgical excision with a stirrup-shaped electrode This instrument makes possible the removal of specimens of a size and shape suitable for frozen sections much the same as in the chemosurgical technic. Unfortunately the tissues are not as satisfactory for section as are the chemically fixed tissues, but if the frozen sections are cut a millimeter or so up from the bottom of the specimens the microscopic structure of the tissue generally is recognizable in spite of the distortion produced by the heat generated by the electrode Very large intraoral lesions may not be amenable to these technics and may require wide surgical excision with the patient under general anesthesia.



Fig. 121 (A) Squamous cell carcinoma of the mucosa of the cheek. (B) Granulation tissue after chemosurgical excision. *(C) Healed lesion. There was no recurrence after five years.*

In the present series of twelve cases of malignant neoplasia there were only three cases in which the cancers were discrete lesions of moderate size Two of these patients were free of cancer after five years and the other showed no evidence of recurrence when she died of other causes after three and one-half years. The rest of the patients were not cured because they either had massive fungating masses which extended through the cheek and were too ex

tensive for a cure to be feasible or they had multiple areas of leukoplakia which developed into more cancers which were not eradicated. One patient had a sarcoma, one an adamantinoma and ten had carcinomas. Eight of the patients with carcinoma were listed as determinate cases and of these patients two were free of cancer after five years or more. Thus, the five-year cure rate was 25 per cent.

During the period covered by these statistics the chemosurgical method was mostly used as a palliative measure to clean up malodorous fungating masses of cancer. However with improvements in the technics for the treatment of intraoral lesions, more neoplasms of moderate size are being treated. If the lesion is not too large for easy chemical hemostasis, the main mass may be excised with a cold knife prior to chemosurgical treatment, but if the mass is large, electrosurgical excision, either alone or followed by chemosurgical treatment, is more readily accomplished. By the use of shorter intervals between chemosurgical excisions, the method may even be used for the removal of cancers of the floor of the mouth or of the tongue. The treatment of such lesions is accomplished by having the patient hold the occlusive dressing in place for the hour's interval which is necessary for the fixative to penetrate far enough to allow the removal of specimens for frozen sections. In some situations it is feasible to remove the main mass electrosurgically, and then to apply the fixative to the walls of the resultant cavity, apply zinc chloride paste impregnated gauze squares, pack the cavity with cotton and spread petrolatum over the cotton to exclude the saliva. Such a dressing often will stay in place for several hours or as long as needed to produce the desired amount of fixation. Although intraoral lesions are more difficult to treat chemosurgically than are lesions on the external surface, the advantages of the microscopic control afforded by the method justify its increased use.

CHAPTER 11

Carcinoma of the Accessory Nasal Sinuses

THE maxillary frontal and ethmoid sinuses are sufficiently accessible for chemosurgical treatment to be feasible The present series is made up of cases in which the carcinoma had already eroded through to the overlying skin so the exposure of the sinuses was accomplished during the removal of the external portion of the neoplasm. However, in less advanced lesions exposure of the sinuses through temporary artificial openings is necessary

Maxillary Sinus

Three patients with carcinoma of the maxillary sinus were treated chemosurgically In each case the carcinoma had eroded through the anterior wall of the antrum and presented a mass on the cheek. Although the primary lesion apparently was eradicated in each case, only one patient survived long enough to be quite sure of this. In this case the patient has remained free of cancer for four years after the removal of an extensive carcinoma (Fig 122) One patient who had an extensive carcinoma (malignancy grade 3) which had eroded into the nasal cavity and into the floor of the orbit exhibited no evidence of primary recurrence when he died six months later of metastases which could not be controlled by dissections of the regional nodes. Another patient who was chemosurgically treated for an extensive, recurrent antral carcinoma died three months later of a febrile disease of undetermined nature there was no evidence of recurrence or metastasis at the time of death.

In the cases of antral cancer treated thus far the approach to the neoplasm has been through the anterior or lateral cheek depending on where the eroding tumor mass presented itself externally However, if the neoplasm should present itself on the palate it would be preferable to work up through this structure. If the neoplasm has not eroded either the cheek or the palate, flaps may be laid back temporarily over the portion of the sinus known to be involved. Possible approaches by this means may be through the cheek, through the supradental fossa (Caldwell Luc approach) or through the palate

At times, excessive mucous secretion tends to interfere with the action of the fixative. For this reason care is exercised to completely wall off the area being treated by means of double-thickness petrolatum gauze strips. If this is not sufficient, parenteral and local atropine may be used to dry up the secretions.

Frontal Sinus

There were no cases of carcinoma which had originated in the frontal sinus in this series. However many cancers of the skin which have invaded the frontal sinuses have been treated successfully by the chemosurgical technic (Fig 10) Therefore, there is no doubt as to the practicality of the chemosurgical treatment of primary carcinoma of the frontal sinus. The only factors limiting the successful treatment of cancer of this structure are invasion through the posterior wall into the cranial cavity or invasion into the ethmoid sinuses and thence into the cranial cavity through the cribriform plate. The latter complication is particularly dangerous because openings in this structure larger than a centimeter in diameter are likely to lead to encephalomalacia and death Invasion through the posterior bony wall of the frontal sinus is less dangerous and openings up to three centimeters in diameter may be tolerated.



Fig 122. (A) Squamous cell carcinoma, grade 3 left maxillary sinus. The circle indicates the location of the palpable portion of the cancer which had eroded through the anterior wall of the sinus. Note that the neoplasm had pushed the eye upward. (B) Lesion during excision of specimens from the sinus. The neoplasm extensively involved the inferior portion of the orbit as far back as the inferior orbital fissure hence, the eyeball was useless and was removed electrosurgically The ethmoid sinuses also were invaded. (C) Reconstruction of the cancer showing medial outgrowths into the ethmoid sinuses (upper) the middle turbinate (middle) and the nasal cavity (lower) (D) Defect after healing. The cavity is lined with sinus mucosa In view of the extensiveness of the ramifications of the cancer the repair was delayed for one year There was no recurrence after four years.

Ethmoid Sinus

Only one patient with carcinoma originating in the ethmoid sinuses was chemosurgically treated. In this case the result was unsuccessful because the cancer not only had invaded the ethmoid the sphenoid sinuses but it had extensively invaded through the cribriform plate and involved the dura over an area four centimeters in diameter The removal of such a large amount of the dura in this area led first to herniation of the cerebral tissue and later to encephalomalacia with exposure of the lateral ventricles and death.

A number of cutaneous carcinomas with invasion into the ethmoid sinuses have been successfully treated, indicating that carcinoma of ethmoid origin should be amenable to chemosurgical treatment if the invasion through the ethmoid plate is not excessive i.e., not over one centimeter in diameter The excision of tissues from the ethmoid region is made difficult by

the numerous paper thin bones which support the walls of the ethmoid air cells However, by the meticulous excision of the specimens and the removal of the bony fragments before sectioning the desired microscopic guidance of excision may be obtained As the cribriform plate is approached progress should be slow and cautious If it becomes evident that this structure has been eroded over an area greater than one centimeter in diameter treatment ordinarily should be discontinued because of the danger of fatal cerebral complications.

CHAPTER 12

Carcinoma of the Larynx

ORIGINALLY there was some doubt concerning the possibility of using the chemosurgical technic in the treatment of carcinoma of the larynx because it seemed likely that the mucous secretions would dilute the fixative chemical and that the cough reflex would disturb the dressings. However an investigation of eight cases carried out in collaboration with the late Dr Wellwood Nesbit and Dr Charles Taborsky of the Department of Otolaryngology has demonstrated that these difficulties are not insurmountable and that the chemosurgical treatment of laryngeal neoplasms is feasible.

Technic

Following the placement of a tracheotomy tube, *exposure of the larynx is accomplished* under local anesthesia by a median laryngotomy (Fig 123A) Usually the grossly visible portion of the carcinoma is removed with an electrosurgical unit prior to the first application of the fixative Over the applied fixative are placed small squares of fixative gauze to help keep the *material in place. Over this is placed a thin* layer of non-absorbent cotton. This, in turn is covered by strips of double thickness petrolatum gauze To prevent aspiration of these strips and of the other dressing materials, the ends of the strips are brought out on the skin and are cut long enough to anchor the dressing firmly *Small* retractors which are used *to hold the* larynx open during the operative procedures are not withdrawn until the wound has been packed tightly with cotton (Fig 123B) This packing serves several purposes it keeps the larynx spread apart preserving good exposure it seals off the larynx keeping out the saliva from above and the mucus coughed up from below and it helps to stabilize the entire dressing A gauze dressing is placed over the cotton and the whole is fastened firmly in place with adhesive tape. Analgesia is obtained with codeine and aspirin or with morphine. Excessive mucous and salivary secretion is prevented by injections of atropine sulfate 1/150 grain (0.4 mg) at six hour intervals. If the lesion involves the epiglottis or the adjacent pharynx or if there is considerable scarring from previous irradiation, aspiration of food is avoided by passing a feeding tube through the nose to the stomach.

Excision of layers of fixed tissue is accomplished by the use of long slender knives and bayonet type nasal forceps (Fig 123C) A beam type of headlight is essential. Usually *two layers are removed daily* one in the early morning and one late in the afternoon. This frequent treatment schedule is advisable because of the rapid separation of fixed tissue from the moist mucous membranes of the larynx and because of the tendency for the dressing to become soaked if left longer Also *it is advisable to complete treatment* as soon as possible because the laryngotomy opening tends to close rather rapidly However it is possible to work through the opening for as long as twenty-four days though exposure tends to become inadequate toward the end of this period. Ordinarily treatment is completed in a few days *and only when the cancer extends* far beyond its expected confines does the period of treatment exceed ten days.

When a cancer free plane has been reached as demonstrated microscopically the area is kept covered with petrolatum gauze until the final layer of fixed tissue has separated (Fig 123D) This usually occurs in two to four days

unless cartilage is involved in which case an extra week is required The packing is continued until the patient has no trouble with aspiration while swallowing this may be a period of a week or two if the carcinoma has patency of the airway through the larynx has been adequately demonstrated by closing the tracheotomy tube with adhesive tape for a day or so The tracheotomy opening ordinarily is allowed to close spontaneously

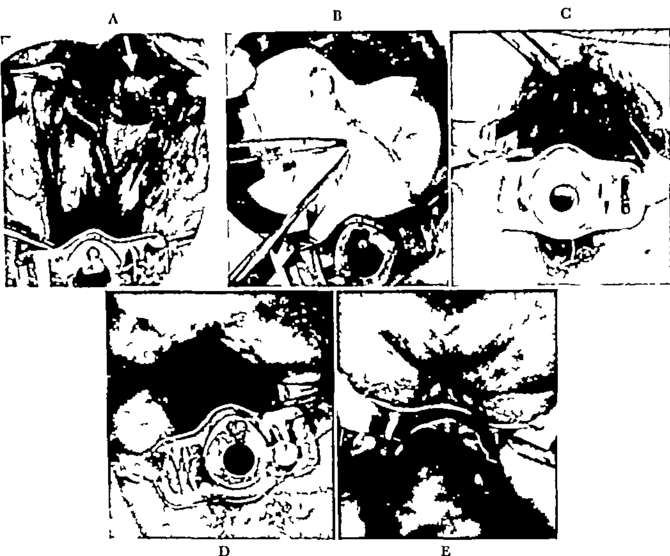


Fig. 123 (A) Squamous cell carcinoma, grade 3 malignancy (Case 8) The largest mass involved the left vocal cord (arrow) but the right true and false vocal cords also were invaded. (B) Dressing showing petrolatum gauze strips and cotton packing in place. (C) Lesion during chemosurgical excision. Note the small retractors, the long handled scalpel and the bayonet type nasal forceps. (D) Granulation tissues after chemosurgical excision of the carcinoma and after removal of the final layer of fixed tissue. (E) Healed lesion. The tracheotomy tube was left in for several weeks. A good airway and husky phonation resulted, but a small focus of carcinoma was thought to have appeared in the supraglottic region after three years. A course of million volt roentgen therapy was given and there was no evidence of carcinoma after two years (five years after chemosurgical treatment)

extended upward into the epiglottis and the pharynx or if there is extensive scarring from previous radiation treatments, but usually it is only a day or two Then the edges of the laryngotomy wound are pulled together with flamed adhesive tapes until healing is complete (Fig 123E) The tracheotomy tube is left in until the

Therapeutic Results

Eight patients with carcinoma of the larynx have been chemosurgically treated and of these two were free of recurrence after four years (25 per cent) These two successfully treated patients were the only ones in whom there

were (1) a primary cancer of reasonably limited extent, and (2) an absence of metastases. Moreover they were the only two patients in whom the cancers were of grade 2 malignancy in the rest the cancers were of grade 3 or grade 4 malignancy

The case summaries of the eight chemosurgically treated cases are as follows

Cases with Successful Results

Case 1 Squamous cell carcinoma, grade 2 malignancy *Duration of symptoms, one year* The mass which was two centimeters in diameter involved the entire right vocal cord. Twenty four chemosurgical excisions were required because of one slender extension which invaded around the posterior wall and into the opposite vocal cord. The last six excisions were carried out on an out patient basis. The laryngotomy wound had closed spontaneously by one month after completion of treatment. There was good phonation although the voice was hoarse. There was no evidence of recurrence after five years.

Case 2 Squamous cell carcinoma, grade 2 malignancy Duration of symptoms, four months. The neoplasm involved the posterior two-thirds of the false cord and extended upward into the epiglottis and adjacent pharynx on the right of the midline. Most of the cancer was removed electrosurgically and a microscopically cancer free plane was reached in one day Because of the involvement of the epiglottis and pharynx there was temporary difficulty with aspiration upon swallowing hence feedings were given by tube. The packing was kept in the larynx for two weeks. Then the wound was pulled together with flamed tapes. The feeding tube was left in for another two weeks. Phonation was good though hoarse. There was no evidence of recurrence in the larynx after four years when a metastasis in a submaxillary node was removed. A subsequent neck dissection by Dr K. E. Lemmer revealed no other cervical metastases.

Cases with Unsuccessful Results

Case 3 Squamous cell carcinoma, grade 3 malignancy Duration of symptoms, six years. Previous treatment included a biopsy and two series of x rays totalling forty-five treatments. A large mass entirely replaced the left vocal cord and invaded most of the right cord as well as the left false vocal cord. The main mass on the left cord was electrosurgically excised. The rest was chemosurgically excised in seven days. The scarring from the radiation resulted in difficulty with aspiration on swallowing. Therefore, the feeding tube was left in and the packing of the larynx was continued for a month. On return for observation after three months the laryngotomy opening had closed completely and there was no evidence of cancer There was insufficient airway to allow removal of the tracheotomy tube, but the patient could talk in a whisper The patient died of a cerebral accident after four months and though there was no evidence of recurrence, the outcome is considered unsuccessful because of the shortness of the period of observation.

Case 4 Squamous cell carcinoma, grade 3 malignancy Duration of hoarseness and dyspnea six months. The patient entered the hospital for an emergency tracheotomy because of extreme dyspnea. A large mass replaced the left vocal cord The main mass was removed electrosurgically and the chemosurgical excisions were completed in seven days. Because the patient's neck was short and thick the use of a feeding tube and special care to wall off the larynx from the mouth was necessary to avoid flooding of larynx during swallowing The wound had closed by two weeks after completion of treatment. The airway through the larynx remained adequate and there was no evidence of recurrence in the larynx after eight months. However a short time later metastases in the cervical and axillary nodes and in the ribs and pelvis were demonstrated.

Case 5 Squamous cell carcinoma, grade 3 to 4 malignancy Duration of hoarseness, six months. The main mass which was over one centimeter in diameter and which affected the anterior three-quarters of the left vocal cord was electrosurgically removed and the rest of the carcinoma was chemosurgically excised in eight days. The final layer of fixed tissue separated two days later except for the fixed cartilage which was removed with a rongeur five days later The lesion had healed by three

weeks after completion of treatment. The air way and phonation were good though the voice was husky Four months later a biopsy was taken by means of suspension laryngoscopy and this revealed residual carcinoma. This focus was removed electrosurgically One month later a metastasis in a left cervical node was noted and roentgen therapy was instituted One year later biopsy again revealed carcinoma in the larynx and more roentgen therapy was given The patient died of the disease three years after the first admission.

Case 6 Squamous cell carcinoma grade 4 malignancy Duration of symptoms, two years. One year before admission an emergency tracheotomy had been done and since the large fungating supraglottic mass was considered inoperable, roentgen therapy was instituted. On laryngofissure the cords were observed to be absent and the thyroid cartilage was exposed in the base of an ulcer three centimeters in diameter on the left side of the larynx. Masses of carcinoma at the inferior and right edges of the ulcer were chemosurgically excised in fourteen days. The feeding tube which was used during treatment was removed after four days. Most of the necrotic cartilage was removed and when seen three months later the area had epithelized. However other foci of carcinoma were present elsewhere in the larynx and in consideration of the patient's poor general condition and the extensiveness of the neoplasm, no further procedures were deemed justifiable

Case 7 Squamous cell carcinoma, grade 3 malignancy Duration of symptoms one and one-half years. The entire right vocal cord and the anterior one-third of the left cord were involved and there was a metastatic mass at the lower edge of the thyroid cartilage The main mass was electrosurgically excised and the rest of the cancer including the metastatic node was removed in eight microscopically controlled stages by the chemosurgical technic. A neck dissection by Dr K. E. Lemmer revealed metastasis in the cervical nodes. After three weeks the laryngeal wound had closed, but after four months the patient returned with recurrence in the larynx, and metastases in the cervical nodes and in the lungs. Roentgen therapy was instituted as a palliative measure.

Case 8 Squamous cell carcinoma grade 3 malignancy (Fig 123A) Duration of symptoms two years. The entire true and false vocal cords on the right and the entire true cord on the left were involved The carcinoma was treated chemosurgically without prior electrosurgical excision of the main mass. Seven excisions were required (Fig 123C) An extra layer from the entire area was removed and sectioned for a double check. The final layer of fixed tissue separated two days after completion of treatment but removal of all the fixed cartilage took another five days (Fig 123D) The wound had healed down to the tracheotomy tube after three weeks (Fig 123E) The airway was adequate and the patient was able to phonate though his voice was husky There was no evidence of recurrence until eighteen months later when a small focus of carcinoma was noticed in the supraglottic region. Million volt roentgen therapy was instituted and there was no evidence of carcinoma five years after the initial treatment.

Comments

Although the use of the chemosurgical method in the treatment of carcinoma of the larynx still is considered to be in the experimental stage, there is no doubt as to its technical feasibility The fact that only two of the eight cases were considered to have a successful outcome does not indicate the method is without value because most of the neoplasms were advanced or had metastasized. Actually the primary lesion presumably was eradicated in four cases (50.0 per cent) but in one case the patient died of intercurrent disease after four months (Case 3) and in one case metastases developed after eight months (Case 4)

In several of the cases there were unpredicted extensions which were microscopically demonstrated to extend for some distance beyond the grossly visible periphery of the cancer The microscopic control of excision made it possible to follow out and eradicate such extensions without the removal of large amounts of uninvolved tissues. This conservatism made it possible to preserve the larynx with an adequate natural airway and with some ability to phonate or at least to whisper In several cases

remarkably good phonation was obtained after the chemosurgical removal of one or even of both vocal cords.

In analyzing the possible causes of the four failures to eradicate the laryngeal cancer the possible presence of neoplastic foci separate from the main mass was considered. Three possible sources of such satellite foci deserve consideration (1) There may have been emboli in the lymphatic vessels around the primary lesion, this is known to occur occasionally in the lymphatics of the skin around melanomas and rarely around squamous cell carcinomas and it is conceivable that it may have occurred around these highly malignant laryngeal cancers. (2) The needle used for injection of the procaine may have passed through the cancer and transplanted a few cells along the needle tract. (3) The tissue steam which resulted from the heat produced by the electrosurgical unit may have resulted in propulsion of cancer cells through the lymphatic channels into the surrounding tissues.

Naturally the chemosurgical technic loses its reliability if foci unattached to the main mass are present. Accordingly in the future it is planned to avoid any possible disseminating factors. Great care will be exercised to inject the anesthetic at a safe distance from the tumor and if the main mass of the cancer is removed *before chemosurgery is instituted* the excision will be done with a cold knife and followed by immediate chemical cauterization. Whether the chemosurgical technic can be unreservedly recommended in the treatment of laryngeal carcinoma will await the results of these investigations.

CHAPTER 13

Neoplasms of the Parotid and Other Salivary Glands

NEOPLASMS of the salivary glands are sufficiently accessible to be amenable to chemosurgical treatment. Although the rare neoplasms of the submaxillary, sublingual and accessory salivary glands may be removed advantageously by the chemosurgical technic, by far the most commonly encountered salivary gland neoplasms are those of the parotid.[43]

NEOPLASMS OF THE PAROTID GLAND

In the treatment of patients with neoplasms of the parotid gland the primary object is the complete eradication of the tumor but an important secondary object is the preservation of the facial nerve. The microscopic control of excision afforded by the chemosurgical technic makes possible an unusually high rate of cure and at the same time makes possible a degree of conservatism that often allows preservation of all or part of the facial nerve.

Technic

The chemosurgical technic as applied to parotid neoplasms is essentially the same as that used in the treatment of other external tumors. Although chemosurgical treatment sometimes is used alone, preliminary surgical removal saves time and reduces discomfort. Therefore the usual procedure is to anesthetize the area and to excise and curet as much of the neoplasm as can be discerned grossly. Often the soft tumor tissue readily yields to the curet but when the normal tissues are encountered the curet meets definite resistance. The surface then is cauterized with dichloracetic acid following which zinc chloride fixative is applied. The layers of fixed tissue usually are excised for sectioning at intervals of twenty four hours, but if the neoplasm is productive of much salivary secretion twice-daily excisions are desirable to avoid soaking of the dressing and dilution of the fixative.

At the beginning of chemosurgical treatment the removal of the neoplastic tissues may be carried out rapidly. However, as the branches of the facial nerve are approached progress must be slow and cautious; only very thin layers of tissue are fixed and excised in order to keep the destruction of uninvolved tissues to a bare minimum. This permits preservation of the facial nerve unless it actually is imbedded in neoplastic tissue. Most parotid tumors arise in the predominant lateral lobe of the gland and unless the neoplasms have been neglected until they have spread deeply they often do not affect the facial nerve. This is particularly true in the lower part of the gland where the nerves are at a comparatively deep level.

In cases in which carcinoma has arisen recently in a mixed tumor of long standing it occasionally may be possible to remove the carcinoma safely although the removal of the mixed tumor might be impossible because of invasion in the vicinity of the internal carotid artery. In such cases it is justifiable to remove the malignant portion and leave the relatively innocuous benign portion. In retrospect, this would have been the better course in the case of one patient who died of complications due to damage to the carotid artery; the carcinoma had been eradicated before the carotid region had been reached and hence it was only during the removal of the deeper benign portion that the artery was damaged.

In cases of carcinoma of the parotid, surgical dissection of the regional nodes is indicated if there is nodal enlargement which is suggestive of metastasis A prophylactic dissection may be recommended even if the nodes are not palpable provided the primary neoplasm is a large highly malignant carcinoma. In some cases it may be advisable to ligate the external carotid artery at the time of the neck dissection in order to avoid the possibility of hemorrhage during chemosurgical treatment of the parotid lesion. Even in the absence of an indication for lymph adenectomy the ligation of the external carotid artery just above the bifurcation may be indicated in cases in which deep invasion around this artery is foreseen. However hemorrhage during separation of the final layer of fixed tissue usually can be prevented more easily by placing a suture-ligature around the artery the pulsation of which may be visualized and palpated in the wound at the completion of chemosurgical excision There were five instances of bleeding sufficient to require a suture ligature or a pressure dressing in the group of thirty two patients treated to date, but these all occurred before the practice of placing suture ligatures was instituted.

Following chemosurgical excision of parotid neoplasms the exposed parotid epithelium secretes saliva for a week or two In most cases the parotid epithelium gradually undergoes replacement by the epithelium of the skin with spontaneous cessation of the drainage. However in cases in which larger salivary ducts are opened, salivary fistulas may form. In several of the earlier cases of this series these fistulas persisted for weeks or months However it was found that the cauterization of the parotid epithelium with dichloracetic acid and a small amount of zinc chloride effected closure of fistulae in every case Even a fistula of twenty one months duration closed within ten days following this treatment Apparently the epithelium of the salivary gland and its ducts is less well adapted to the conditions on the body surface than is the epithelium of the skin. Hence, if the latter is given a chance to compete on even terms it will replace the parotid epithelium. After chemosurgical treatment there were no instances of the Frei syndrome (flushing and sweating over the parotid and temporal areas during eating)

Carcinoma of the Parotid Gland

In general, carcinomas of the lower pole of the parotid gland are less likely to involve the facial nerve than those in the upper portions. Hence even rather large, and deep seated masses may be removed from this region without producing facial paralysis (Fig 124) The removal of extremely large cancers from this region may necessitate the interruption of the mandibular branch of the facial nerve but since this only affects the innervation of the lower lip the deformity is not noticeable (Fig. 125)

Deeply situated carcinomas in the midportion of the gland are likely to have invaded around the main trunks of the facial nerve and in such cases there is no choice other than to interrupt the nerve (Fig 126) However even in such cases it is worthwhile to use the greatest care to avoid destruction of any of the uninvolved portions of the nerve because some pathways may be spared and there may be some degree of return of function. The maximal restoration of function may not take place for as much as a year or two The exact mechanism of this partial restoration of nerve function is not always clear but at any rate it occurs often enough to encourage the exercise of the greatest possible conservatism.

Carcinomas in the preauricular portion of the parotid gland tend to involve parts of the facial nerve at a relatively early stage (Fig 127) However in this region too the conservatism of the chemosurgical method is valuable because some branches may be found to be uninvolved.

Carcinomas in the preauricular portion of the parotid gland may invade the temporomandibular joint, but this is not a serious complication. Often it is possible to remove the invading malignant tissue without appreciable impairment of the function of the joint. Ankylosis never develops. Even removal of the condyloid process the articular disk and portions of the adjacent temporal bone causes no more difficulty than moderate malocclusion because the attached muscles and ligaments tend to keep the structure in place.

Some parotid carcinomas invade the ear, especially in the vicinity of the external auditory canal where extensions may follow along the surface of the bones and cartilages of this structure (Fig 124) Such infiltrations may be followed out readily by the chemosurgical technic. Only rarely does stenosis of the external auditory canal develop the care of this complication is discussed in the chapter on carcinoma of the ear

Carcinomas in the postauricular portion of the parotid tend to invade deeply along the anterior edge of the mastoid bone. Often the facial nerve is affected but there may be a slight but important return of function if the damage to the nerve is kept to a minimum (Fig 128)

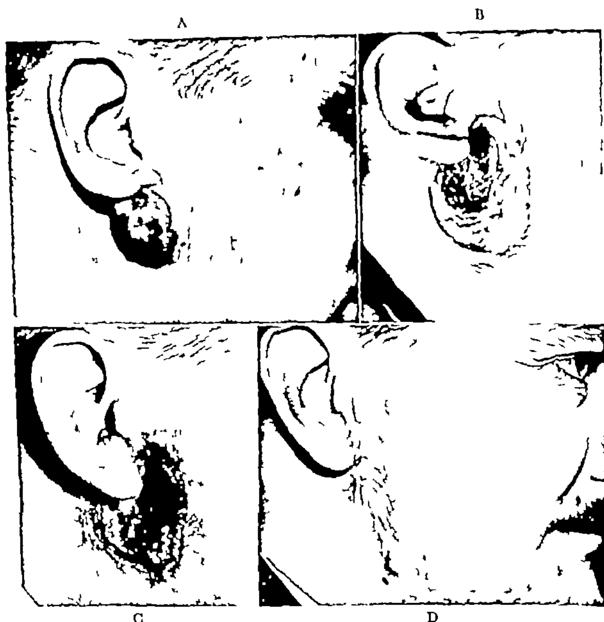


Fig 124 (A) Mucoepidermoid carcinoma of the parotid. (See Fig 129A.) The ulcerated protrusion from the underlying main mass had appeared after an operation for purposes of exploration and biopsy A small dose of roentgen rays had produced no visible benefit. (B) Granulation tissue and fixed tissue at completion of chemosurgical treatment. The carcinoma went beyond the confines of the gland in several places one extension followed the perichondrium of the cartilages of the external auditory canal (C) Lesion after separation of the fixed tissue The mottled appearance of the central granulation tissue was caused by islands of parotid epithelium growing on the granulation tissue (D) Healed lesion. Note the absence of facial paralysis despite the close approach to the nerve There was no recurrence after seventeen years.



Fig 125 (A) Squamous cell carcinoma of the parotid gland. (See Fig. 129B) (B) Granulation tissue after chemosurgical excision. Some fixed tissue is still adherent over the sternocleidomastoid muscle. The posterior edge of the ramus of the mandible is exposed. A slender extension of cancer followed the epimysium of the stylohyoid muscle (C) Healed lesion. The facial nerve was not interrupted except for the unimportant mandibular branch. There was no recurrence when the patient died of other causes after twelve years.



Fig 126. (A) Carcinoma of the parotid. (See Fig 129C.) The lesion had recurred after excision and roentgen therapy one year before. (B) Granulation tissue after chemosurgical excision. The moderately infiltrative carcinoma (Fig 129C) surrounded the main branches of the facial nerve necessitating their interruption. The inferior wall of the external auditory canal also was extensively invaded. (C) Healed lesion three months later Note the linear scar There was no recurrence after seven years.



Fig 127 (A) Carcinoma of the preauricular portion of the parotid gland. The facial muscles of the upper lip, lower eyelid and forehead had been paralyzed for six months. (B) Granulation tissue after chemosurgical excision. The innervation of the lower part of the mouth was preserved so there was no sagging (C) Healed preauricular lesion after eighteen months. A postauricular focus of carcinoma of the same type had appeared. Whether this was a separate primary neoplasm or a metastasis from the preauricular lesion was not clear but the former seems most likely At any rate the new mass was chemosurgically excised and following this a neck dissection, which revealed metastatic nodes, was done by Dr Otto Hibma. There was no recurrence after six years.

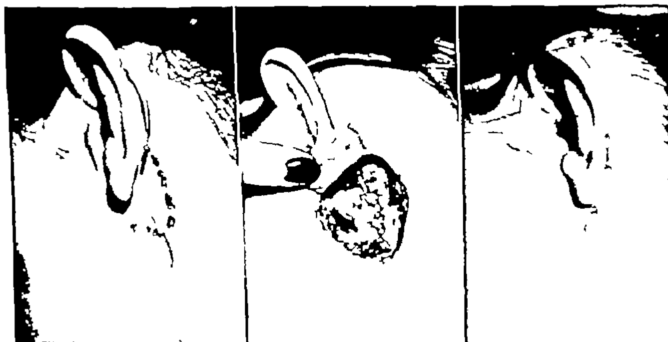


Fig 128 (A) Carcinoma of the parotid, recurrent after surgical excision and insertion of radium needles. (B) Granulation tissue after chemosurgical excision. The mastoid process was exposed. There was complete paralysis for a year after which function slowly returned to the muscles of mouth and forehead but not to the lower eyelid. (C) Healed lesion. The small salivary fistula just below the lobe of the ear was cauterized with dichloracetic acid and zinc chloride fixative 12 days later the fistula was healed. There was no recurrence after ten years.

The thin capsule of the parotid gland does not appreciably hinder the spread of carcinoma. In every case in this series there was invasion into the tissues surrounding the gland. The invading outgrowths tend to infiltrate in an irregular manner along tissue planes which offer diminished resistance to the particular neoplasm. The most striking example of this tendency is exhibited in the cases in which there is selective affinity for the nerve sheaths. This phenomenon was observed in 28.0 per cent of the parotid carcinomas which have been treated to the date of this writing. In one case the spread of the neoplasm outward from the main mass in the preauricular region was exclusively localized in the epineurium and perineurium of the facial nerves; in these sheaths the cancer reached as far as the rim of the orbit and the angle of the mouth. The significant point about these outgrowths is the fact that many are of such small caliber that their presence often is entirely unsuspected on the basis of clinical examination alone; hence, their certain detection *can be accomplished only by the microscopically* controlled excisions afforded by the chemosurgical technic. It is probable that most recurrences following surgical excision are due to the failure to recognize and eradicate such extensions; very few recurrences are attributable to multiple foci because this phenomenon is very rare in the parotid gland.

Therapeutic Results in Cases of Carcinoma of the Parotid Gland

In the group of thirteen cases of carcinoma of the parotid gland observed for five years or more there were two cases in the indeterminate group and eleven cases in the determinate group. The five-year cure rate in the determinate group was 54.5 per cent (Table XLII).

The effect of the size of the lesion on prognosis is considerable. Thus, while 100 per cent of the patients with lesions under 4 cm. in average diameter were cured only 37.5 per cent of those over 4 cm. were successfully treated (Table XLIII). Because most of the parotid neoplasms were relatively large, it will be noted that the size of the lesions in the four classifications are double those which have been used for neoplasms in other regions. Examples of carcinomas in the various groups are as follows: group B (diameter 2 to 4 cm.) in Figures 124, 127 and 128; group D (diameter 6 cm. or more) in Figures 125 and 126.

TABLE XLII

FIVE-YEAR END RESULTS FOR CARCINOMA OF THE PAROTID GLAND

This series includes the cases of all patients with histologically proved carcinoma of the parotid, both early and advanced, previously untreated and recurrent, with and without metastasis, who were chemosurgically treated during the twelve year period ending six years prior to this writing.

Total number of cases	13
Indeterminate group: total number	2
Patients dead from other causes without recurrence	1
Patients lost from observation without recurrence	1
Determinate group: total number	11
Unsuccessful results, total number	5
Patients dead, cancer present at death	5
Patients lost from observation with cancer	0
Patients living with cancer	0
Successful results, patients free from cancer for five years or more	6
Five-year rate of cure (6 ÷ 11) × 100	54.5%

TABLE XLIII

EFFECT OF SIZE OF CARCINOMA OF THE PAROTID GLAND ON FIVE-YEAR END RESULTS

Group	Average Diameter Cm.	Number of Lesions	Successful Results Number	Successful Results Per cent
A	under 2	0		
B	2 to 4	3	3	100.0
C	4 to 6	3	1	33.3
D	6 or more	5	2	40.0

It is not the neoplasm's extensiveness per se that reduces the curability of patients with large parotid carcinomas. Rather it is the increased chance of metastasis and of involvement of vital structures. Thus, in this series in which there were five unsuccessfully treated patients there were two failures attributable to metastasis, one failure owing to extremely extensive permeation along the facial nerve sheaths, one failure because of death from pulmonary edema and bronchopneumonia in a patient who was in very poor condition when therapy of an extremely advanced parotid tumor was instituted and one failure from damage to the common carotid artery during excision of a cancer which eroded that vessel. Therefore if there has been no complication such as metastasis or involve-

ment of the internal carotid artery it is possible to chemosurgically excise even the very large neoplasms

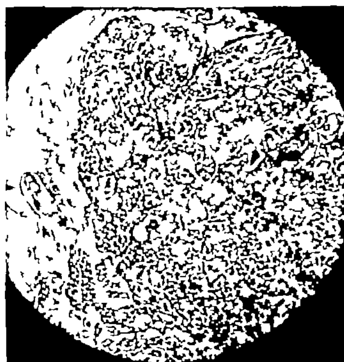
The effect of previous treatment on prognosis is not appreciable as far as is indicated by the present small series. Thus, in the group of seven patients in whom previous treatment had been received there were four who were cured (57 0 per cent) while in the group of four patients who had received no previous treatment two were cured (50 0 per cent) Too much significance should not be attached to the statistics of such a small series, but the data do indicate the special usefulness of the chemosurgical technic in the treatment of recurrent lesions because these otherwise would carry a very poor prognosis. Actually previous treatment would be expected to impair prognosis somewhat because of the delay occasioned by the unsuccessful treatment and possibly because of the dissemination of neoplastic cells by unsuccessful surgical treatment. It is noteworthy that 63 6 per cent of the patients in the present series had received previous unsuccessful surgical or radiation treatment.

The effect of the histologic grade of malignancy on prognosis is not readily expressed because there is no generally accepted system of grading that is applicable to all of the various types of parotid carcinoma. However, there was a definite correlation between the degree of invasiveness of the various carcinomas and the prognosis. Thus, five of six patients who were considered to have "moderately invasive carcinomas" were successfully treated (83.3 per cent) while only one of five patients who had "highly invasive carcinomas" were successfully treated (20 0 per cent) The "moderately invasive" lesions were the following types of carcinoma malignant mixed tumor two cases squamous cell carcinoma grade 3 one case (Fig 129B) mucoepidermoid carcinoma, one case (Fig 129A) cylindroma one case (Fig 129C) and acinic cell carcinoma one case The "highly malignant" carcinomas were of the following types malignant mixed tumors, two cases undifferentiated carcinoma, two cases and squamous cell carcinoma, grade 4 one case

A better way of expressing the prognosis would be to tabulate the results of treatment for each pathologic type of carcinoma but the present series is too small to permit definite conclusions However the results are suggestive and they fall in line with the behavior of these neoplasms as described by others[22] Thus the tumors that usually are not very highly malignant—mucoepidermoid carcinoma (Fig. 124) cylindroma (Fig 126) and acinic cell carcinoma—all were successfully removed The more dangerous squamous cell carcinoma was eradicated in the case in which the degree of malignancy was grade 3 (Fig 125) but was not eradicated in the case in which the malignancy was grade 4 The highly malignant undifferentiated carcinomas also are considered dangerous and in this series one was successfully removed (Fig 127) but one was not. The prognosis in malignant mixed tumors depends to a considerable extent upon the degree of malignancy of the malignant component In the four cases of this type in this series there were two cases of highly malignant undifferentiated carcinoma and two cases of moderately malignant adenocarcinoma. One of the latter group was successfully removed (Fig 128) but the rest were not eradicated either because of metastasis or because of excessively advanced local spread.

The effect of the site of origin on prognosis is not appreciable as long as the neoplasm arises in the lateral lobe. Thus, in a group of nine cases of carcinoma of the retromandibular area, five had a successful outcome (55 6 per cent) while in a group of two cases of carcinoma of the preauricular region, one had a successful result (50 0 per cent) However it should be pointed out that neoplasms arising in the deep lobe of the parotid, medial to the facial nerve, have a greater chance of invasion of the internal carotid artery and the jugular vein. One such case is included in this series, and because the neoplasm eroded the internal carotid artery the elderly patient developed a thrombosis with consequent hemiplegia, convulsions, coma and death there also was hemorrhage from the vessel but this was controlled and was not the cause of death However in a recent case in which the neoplasm was followed into the lateral pharyngeal space there was no damage to the internal carotid artery which was situated just posterior to the neoplasm The artery is

A



B C

Fig. 129 Parotid carcinoma. The tissues were fixed in situ with zinc chloride (A) Mucoepidermoid carcinoma from the patient shown in Figure 124 (B) Squamous cell carcinoma, grade 3, from the patient shown in Figure 125 The large, clear cells are degenerated rather than keratinized. (C) Cylindroma from the patient shown in Figure 126.

protected to some degree by the inflammatory swelling which tends to push the vessel away from the site of application in addition the rapid flow of blood through the artery tends to dilute the fixative and hence to reduce the danger of permeation through the vessel wall

The effect of metastasis on prognosis in cases of carcinoma of the parotid gland is profound but fortunately the incidence of metastasis tends to be relatively low in patients with parotid carcinoma In this series there were three patients with metastasis and of these one was cured (33 0 per cent) In the group of eight patients without metastasis, six were cured (75 0 per cent)

Comparison of Results with Those of Other Authors

The five year cure rate of 54.5 per cent achieved by the use of the chemosurgical technic exceeds the best rates reported in the literature with few exceptions (Table XLIV) The series with a rate of 63 6 per cent[18] was based on results in a series of cases in which the proportion of smaller cancers (under four centimeters in diameter) was twice as great as in the present series of patients treated chemosurgically (56 0 per cent as compared with 27 0 per cent) The present series is by no means one in which there was a selection of well demarcated readily accessible operable carcinomas. On the contrary, a number of the patients had cancers which ordinarily would be considered inoperable

The unusually high rate of cure was a result of the microscopic control of excision provided by the chemosurgical technic. The microscopic control also made possible a considerable degree of conservatism because only one or two millimeters of normal tissue had to be removed beyond the farthest extent of the carcinoma. This conservatism in turn, resulted in the preservation of part or all of the facial nerve in nearly half of the patients (in five of the eleven patients in the determinate group) This was the case in spite of the fact that three patients had paralysis before the institution of chemosurgical treatment. Most authors give insufficient data to allow accurate comparison with regard to the incidence of postoperative paralysis. However in a group of large carcinomas such as those which comprise the present series it is

TABLE XLIV

COMPARISON OF THE FIVE-YEAR END RESULTS OF CHEMOSURGICAL TREATMENT OF CARCINOMA OF THE PAROTID GLAND WITH THE END RESULTS OF OTHER AUTHORS

Author	*Treatment*	*Number of Determinate Cases*	*Successful Results*	
			Number	*Per cent*
Mohs	Chemosurgery	11	6	54 5
Buxton, Maxwell and Cooper[18]	Surgery (plus roentgen therapy in some cases)	33	21	63 6
Ariel Jerome and Pack[1]	Surgery	24	10	41 7
		12*	10	83 3
Jerome[88]	Surgery	13	6	46 1
Ahlbom ‡	Surgery plus radium	81	27	33 3
Swinton and Warren [3]	Surgery	6	2	33 3
Quattlebaum, Dockerty and Mayo[78] †	Surgery (plus roentgen therapy in some)	19	6	31 6
Taylor and Garcelon[77]	Surgery	26	5	19 2
Smith and Stenstrom[44]	Surgery and roentgen therapy	35	4	11 4
Stein and Geschickter[88]	Surgery	21	3	14 3
Benedict and Meigs	Surgery	30	1	3 3
Wakeley [81]	Surgery	12	0	0
Martin[44]	Radiation	6	0	0

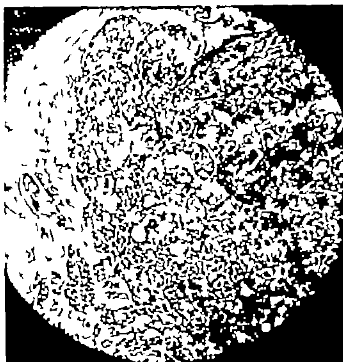
Patients thought to be incurable at the first visit are excluded from this group

† Adenocarcinoma of "cylindroma" type only

‡ More recent but incomplete statistics from the Radiumhemmet give a rate of cure of 61 per cent.[77]

Note Edvall[77] recently reported only 12.8 per cent recurrences in a series of malignant salivary gland tumors but since the proportion of indeterminate and determinate cases was not given the rate of cure cannot be expressed.

A







B C

Fig 129 Parotid carcinoma. The tissues were fixed in situ with zinc chloride. (A) Mucoepidermoid carcinoma from the patient shown in Figure 124 (B) Squamous cell carcinoma, grade 3 from the patient shown in Figure 125 The large, clear cells are degenerated rather than keratinized. (C) Cylindroma from the patient shown in Figure 126.

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			Number	*Per cent*
Mohs	Chemosurgery	11	6	54.5
Burton, Maxwell and Cooper[14]	Surgery (plus roentgen therapy in some cases)	33	21	63.6
Ariel, Jerome and Pack[10]	Surgery	24	10	41.7
		12	10	83.3
Jerome[38]	Surgery	13	6	46.1
Ahlbom ‡	Surgery plus radium	81	27	33.3
Swinton and Warren[83]	Surgery	6	2	33.3
Quattlebaum, Dockerty and Mayo[74]†	Surgery (plus roentgen therapy in some)	19	6	31.6
Taylor and Garcelon[87]	Surgery	26	5	19.2
Smith and Stenstrom[84]	Surgery and roentgen therapy	35	4	11.4
Stein and Geschickter[86]	Surgery	21	3	14.3
Benedict and Meigs[1]	Surgery	30	1	3.3
Wakeley	Surgery	12	0	0
Martin[64]	Radiation	6	0	0

Patients thought to be incurable at the first visit are excluded from this group.

† Adenocarcinoma of "cylindroma" type only

‡ More recent but incomplete statistics from the Radiumhemmet give a rate of cure of 61 per cent.[77]

NOTE Edvall[17] recently reported only 12.8 per cent recurrences in a series of malignant salivary gland tumors but since the proportion of indeterminate and determinate cases was not given the rate of cure cannot be expressed.

robable that with surgical excision the inci-
ence of total paralysis would have been nearly one hundred per cent because in every case radical resection would have been necessary

Mixed Tumor of the Parotid Gland

In the absence of previous unsuccessful surgical or radiation treatment, mixed tumors of the parotid gland often present discrete, well defined masses hence they frequently are amenable to surgical procedures of the usual type. It is for that reason that the present series includes only five cases of mixed tumor in contrast to the thirteen cases of carcinoma of the parotid.

Of course accurate differentiation between mixed tumor and carcinoma is not always possible by clinical examination alone. This is particularly true when the neoplasm is recurrent and of long duration because there may be considerable fixation and induration from the scar tissue. When there is reasonable doubt of the benign nature of the tumor chemosurgical excision is preferable. Even if the neoplasm proves to be a mixed tumor nothing is lost except, perhaps the few extra days required for chemosurgical treatment.

The technic for the chemosurgical excision of mixed tumors is essentially the same as for carcinoma of the parotid gland. However the tumor mass usually stands out more distinctly from the normal parotid gland tissue than does carcinoma. This makes it more easy to excise and curet out the main mass prior to the institution of chemosurgical treatment.



Fig 130 (A) Mixed tumor of the parotid gland. (B) Patient after chemosurgical excision. Note the absence of facial paralysis. There was no recurrence after nine years.

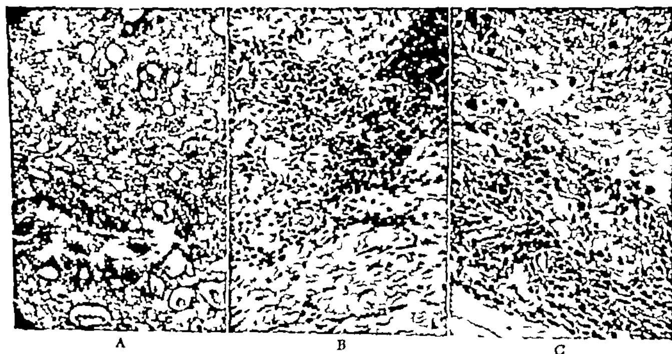
In the absence of previous treatment mixed tumors tend to exhibit a globular configuration without unexpected outgrowths into the surrounding tissues (Fig 130) However lesions which have recurred after previous excisions may have more irregular outlines and they may present small, unpredicted outpouchings which might be overlooked if the microscopically controlled chemosurgical technic were not used (Fig 131) The characteristic microscopic features of mixed tumors permit ready differentiation from normal parotid tissue and from other tumors (Fig 132)

Successful results were achieved in all five



A B C

Fig. 131 (A) Mixed tumor of the parotid gland with extension into the submaxillary region. The tumor had recurred after two surgical excisions and one course of six roentgen treatments. (B) Granulation tissue after chemosurgical excision. Fixed tissue was still adherent to an area below the ear where a deep unpredicted extension had been followed to its termination. The herniated tissue at the lower edge of the lesion was a lobule of submaxillary salivary gland. (C) Healed lesion. Note the absence of facial paralysis except for the unimportant mandibular branch. There was no recurrence after five and one-half years.



A B C

Fig. 132. (A) and (B) Photomicrographs of mixed tumor from the parotid gland of the patient shown in Figure 130. (C) Mixed tumor from the patient shown in Figure 131.

of the cases of mixed tumor treated during the twelve year period which ended five years prior to the date of this writing Two of the patients were free of recurrence after nine years and three were well after more than five years. No facial paralysis was produced except in one patient in whom the unimportant mandibular branch was interrupted (Fig 131) and in one patient in whom the branch to the forehead was permanently paralyzed. In the latter patient there was complete facial paralysis for several months but this gradually improved until only the forehead was affected.

During the five years preceding this writing five more mixed tumors have been excised chemosurgically with successful results in all cases after intervals of one to five years. Facial paralysis developed in one patient who had an unusually deep-seated tumor

One papillary cystadenoma lymphomatosum (Warthin's tumor) was chemosurgically excised and there was no evidence of recurrence after two years. Also there was one case of sarcoid of the parotid gland the patient had no recurrence after six years.

NEOPLASMS OF OTHER SALIVARY GLANDS

Submaxillary Gland

Carcinoma of the submaxillary gland was encountered only once and in this case the recurrent neoplasm in the submaxillary gland was eradicated but the patient developed cervical metastases which could not be controlled by surgical dissection and roentgen therapy

No mixed tumors of the submaxillary gland have been observed in the Chemosurgery Clinic.

Submental Gland

Carcinoma or mixed tumor of the submental salivary gland should respond well to chemosurgical treatment, but no cases had been encountered up to the time of writing A number of cutaneous neoplasms which have invaded both the submental and submaxillary glands have been chemosurgically excised without difficulty therefore, it is likely that neoplasms originating in these structures also would be amenable to this type of treatment.

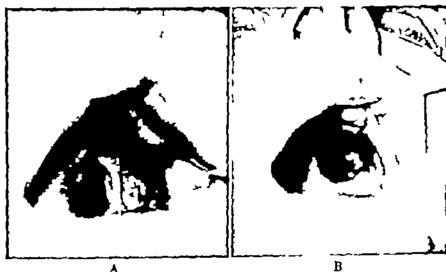


Fig 133 (A) Defect in the palate immediately after removal of an adenocarcinoma which had arisen in a mixed tumor of the palatal salivary glands and which not only invaded through the bone of the palate into the antrum and nasal cavity but also eroded the medial pterygoid plate of the sphenoid bone. (B) Healed lesion six months later The defect had reduced to one-quarter its original diameter A denture with an obturator effectively closed the opening There was no recurrence after five years.

Accessory Salivary Glands

Occasionally salivary gland tumors arise in accessory salivary glands which may be in the mouth or in adjacent tissues. One such neoplasm a carcinoma which arose in the palate and developed into a large mass, was successfully treated by means of chemosurgical excision which was carried out by an approach through the hard and soft palate (Fig 133) Another salivary gland carcinoma (cylindroma) which arose in the nasal mucosa had recurred after many surgical and radiation procedures Upon chemosurgical excision the neoplasm was found to have extended back to the soft palate into the medial orbit, into the ethmoid sinuses and other adjacent tissues A year later residual foci in the superior turbinate and ethmoid regions were found by Dr Richard Shepard, and since there was invasion in the region of the cribriform plate he considered it advisable to stop chemosurgical treatment at an optimum palliative level rather than to undertake the hazardous procedure which would be necessary to give any chance of eradication of the neoplasm.

Cutaneous mixed tumors of salivary gland type are discussed in the chapter on benign tumors of epithelial origin.

CHAPTER 14

Postoperative Recurrences of Carcinoma of the Breast

RADICAL mastectomy is the treatment of choice for primary carcinoma of the breast because this operation gives the best chance of complete removal of metastatic foci in the regional nodes and in the intervening lymphatics. Some postoperative recurrences, however may be treated advantageously by the chemosurgical technic. Most recurrent mammary carcinomas are rather highly invasive neoplasms which extend surprisingly far into the surrounding tissues hence, the microscopic guidance of excision afforded by the chemosurgical method is valuable in the demonstration of the exact extent of these infiltrations. In view of the thinness of the chest wall, the conservatism which may be safely practiced with the chemosurgical technic also is advantageous because obviously in this region it is impossible to remove wide margins of uninvolved tissues.

The limiting factor in the chemosurgical treatment of recurrent nodules is invasion of the pleura. In the absence of pleural invasion it is possible to remove the nodules even though they have invaded the intercostal muscles, the ribs, the costal cartilages or the sternum (Fig 134A) However if the pleura is invaded there is little chance of eradicating the disease (Fig 134B) Usually the cancer invades most deeply through the intercostal muscles the bone and cartilage are not invaded until the neoplasm is rather advanced.

During chemosurgical treatment, care must be exercised to avoid penetration of the pleura. This requires meticulous care as the pleura is approached. The swelling produced by the chemical inflammation tends to increase the thickness of the tissues somewhat but this adds only a few millimeters to the effective thickness and cannot be counted on too strongly In the present series, sections of ribs and the full thickness of intercostal muscles have been removed in a number of cases but in none was the pleura penetrated by the fixative.

A total of fourteen patients with mammary carcinoma have been chemosurgically treated. Of these five had recurrent nodules which seemed to be sufficiently limited for complete chemosurgical excision to be possible. However only two were successfully treated one had had no recurrence after two years but had developed a deeply invasive nodule in another area (Fig 134) the other was well after eight years. The three unsuccessfully treated patients proved to have carcinomatous invasion into the pleura and hence treatment was carried as far as safely possible and then discontinued. Significant palliative benefits were obtained in the unsuccessfully treated patients.

Massive inoperable masses of mammary carcinoma were chemosurgically excised for palliative purposes in five patients. The elimination of foul smelling, infected, bleeding masses was accomplished but the neoplasms regrew and were fatal in every case. It was questionable whether the palliation was sufficient to justify the chemosurgical treatment of these patients.

Although chemosurgical treatment of primary carcinoma of the breast is not recommended, four patients with previously untreated lesions were accepted. This was done for different reasons in each case. In one case the patient refused radical mastectomy because she had developed pneumonia after each of several operations she had previously had however she

agreed to chemosurgical amputation of the breast. The primary lesion was eradicated but after six years axillary and distant metastases suddenly became active and caused the patient's death. In the second case an extensive inoperable cancer had been chemosurgically excised from the left breast area for palliative the carcinoma was chemosurgically excised and after one month when she had regained some strength the metastatic nodules in the axilla were surgically dissected by Dr James Neller. Axillary and mediastinal nodes appeared after three years and the patient died after six years but there was no recurrence at the primary site



Fig 134 (A) Mammary carcinoma which had recurred after radical mastectomy and postoperative roentgen therapy The circle around the nodule indicates the zone of induration. (B) Healed lesion two years later A new mass had appeared over the sternum and had been neglected until it had become inoperable because of pleural involvement.

purposes and shortly afterwards a new primary in the right breast was noticed. This was chemosurgically excised but the patient was followed for no longer than six weeks because of the hopelessness of her condition. In the third case the patient was so emaciated that it was believed that she would not tolerate a radical mastectomy. Moreover the fungating mass was firmly fixed to the chest wall. For these reasons The fourth patient had a nodule in the skin near the sternal notch. Since the neoplasm was believed to have arisen in the skin or skin appendages it was chemosurgically excised. However the neoplasm proved to be a mammary carcinoma which extended to both sides of the midline. Removal was complete as revealed by the absence of carcinoma in the specimen subsequently removed by radical

mastectomy There was no recurrence after three years.

In conclusion it should be emphasized that chemosurgery in the treatment of carcinoma of the breast ordinarily is limited to the removal of postoperative recurrent nodules. Inasmuch as there is little chance of cure if there is involvement of the pleura, every effort should be made to detect recurrences at the earliest possible moment. If this is done the chances of eliminating recurrent foci by means of the chemosurgical technic are very good.

CHAPTER 15

Carcinoma of the Penis and Scrotum

ALTHOUGH neoplasms of the penis and scrotum ordinarily come within the field of genitourinary surgery the advantages of microscopically controlled excision not infrequently bring these lesions within the realm of chemosurgery

Carcinoma of the Penis

Inasmuch as most carcinomas of the penis arise on the glans or on the prepuce and inasmuch as most of these neoplasms remain localized to the distal portion of the penis for a considerable time these lesions should almost always be amenable to conservative chemosurgical treatment. There would seem to be little justification for amputation of the penis when the carcinoma affects only the distal portion of the organ perhaps the reason for the frequency of this operation stems from the mistaken belief that the carcinoma often extends by continuous permeation through the lymphatic vessels of the shaft of the penis. Actually if carcinoma spreads to the regional lymph nodes it is much more likely to go by way of embolism rather than by continuous permeation.

The chemosurgical technic as applied to penile lesions is much the same as elsewhere on the surface of the body Preliminary surgical excision of the main mass after blocking the penile nerves effectively reduces the treatment time and minimizes the discomfort. If the lesion does not affect the urethral os no catheter is necessary because although there may be edema from the action of the fixative chemical there ordinarily is no appreciable obstruction of urinary flow However it is advisable to avoid placing adhesive tapes completely around the penis because with the development of edema this might impede the flow of urine and, more importantly it might produce circulatory impairment which possibly could eventuate in gangrene Postchemosurgical wounds of this portion of the penis usually heal without appreciable deformity (Fig 135) Even if the entire circumference of the prepuce should require removal the resulting scar does not produce sufficient constriction to cause appreciable reduction in the size of the urinary stream (Fig 136) Only if the lesion covers a rather large area and involves one side of the urethra does there develop much change in the direction of the urinary stream (Fig 137) If the carcinoma affects the glans around the meatus an indwelling catheter is employed until active chemosurgical treatment has been completed (Fig 138) Superficial carcinoma such as that arising in erythroplasia of Queyrat may be removed with conservatism corresponding with the limited invasion (Fig 139)

Therapeutic Results in Cases of Carcinoma of the Penis

Seven patients with squamous cell carcinoma of the penis were chemosurgically treated during the twelve year period which ended six years prior to this writing and all were followed for five years or more Successful results were obtained in five patients. Therefore the five-year cure rate was 71 4 per cent. There were two failures one because of a sudden coronary occlusion shortly after treatment of an extensive recurrent lesion and one because of uncontrolled inguinal and distant metastases

Most of the lesions in this series were fairly large There was one patient in group B (average diameter 1 to 2 cm) three in group C (2 to 3 cm.) and four in group D (over 3

Fig 135 (A) Squamous cell carcinoma of the prepuce and retroglandular sulcus. The degree of malignancy was grade 3 (B) Fixed tissue at completion of chemosurgical excision. The lines show the origin of the six specimens which had been removed for frozen section. (C) Granulation tissue after separation of the final layer of fixed tissue (D) Healed lesion. There was no appreciable deformity *There were small palpable inguinal nodes but an inguinal dissection* revealed no metastasis. There was no recurrence after five years.



Fig 136. (A) Squamous cell carcinoma, grade 2. The growth affected the entire circumference of the prepuce but varied considerably in the depth of invasion in different areas of the glans. (B) Granulation tissue after chemosurgical excision. (C) *Healed lesion. There was no appreciable limitation of urinary flow* either from the edema during treatment or from the scar contraction later There was no recurrence after thirteen years when a new carcinoma developed in the keratotic epithelium at the tip of the glans.

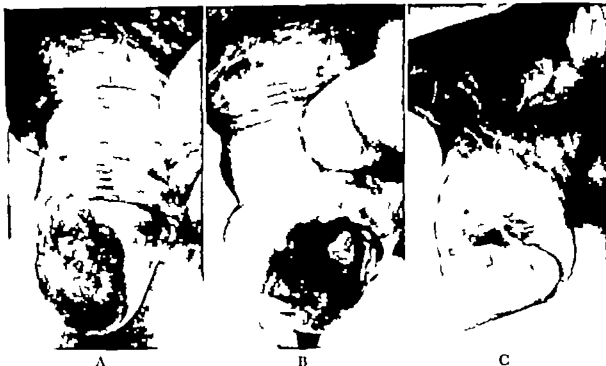


Fig. 137 (A) Squamous cell carcinoma, grade 2. The entire right half of the glans was involved. (B) Granulation tissue after chemosurgical excision of the cancer which invaded the urethra. The most proximal extension was in the perineurium of one nerve (C) Healed lesion. There was no recurrence after five years.



Fig. 138 (A) Squamous cell carcinoma, grade 1 with involvement of the entire glans in a patient twenty-one years of age The neoplasm had recurred after two electrosurgical excisions. (B) Granulation tissue after chemosurgical excision. (C) Healed lesion. The functions of the organ were not impaired There was no recurrence after six years.

cm.) The unsuccessfully treated patients both had lesions over 3 cm. in diameter

Two patients had metastases and both died of their cancer while all of the five patients without metastases were cured.

Other neoplasms of the penis besides squamous cell carcinoma also may be treated chemosurgically Basal cell carcinoma is rare and there are no cases in the present series.

amount of invasion of the pubic or perineal region is suspected the chemosurgical technic probably would be of value.

Carcinoma of the Bladder

Although no patients with primary bladder carcinomas have been chemosurgically treated up to the time of this writing it is planned to



Fig 139 (A) Squamous cell carcinoma, grade 2, arising in erythroplasia of Queyrat. (B) Granulation tissue after chemosurgical excision. (C) Healed lesion. There was no recurrence of the carcinoma or of the erythroplasia after six years.

One patient with condyloma accuminata in the urethral meatus was successfully treated.

Carcinoma of the Scrotum

Scrotal neoplasms are relatively rare. Only one patient with this condition has been treated chemosurgically After removal of his basal cell carcinoma the wound healed with a practically invisible scar and the lesion had not recurred after five years In this case there was no invasion of the testis but if there were this should not have led to complications during treatment or during healing

No testicular neoplasms have been chemosurgically treated Although it is possible that certain of these might be treated to advantage it is probable that, in view of their dependent position, most of them would be more easily removed surgically In cases in which a certain

cooperate with the urology department in an investigation of the feasibility of using this technic for certain infiltrative lesions. A preliminary cystostomy with the placement of ureteral catheters would make it possible to obtain adequate exposure and a reasonably dry field during the period of treatment. Upon completion of active chemosurgical treatment the surface would not have to be kept dry However it would be necessary to maintain the cystostomy opening for several days until the final layer of fixed tissue could be removed. In one case of deep-seated carcinoma of the skin of the pubic area the bladder was opened into chemosurgically without untoward results other than the fistula. However a decision as to the practicality of using this method in the treatment of carcinoma elsewhere in the bladder must await clinical trial.

CHAPTER 16

Carcinoma of the Vulva, Vagina, Urethra and Cervix

GYNECOLOGIC conditions which from a technical standpoint are amenable to emosurgical treatment are carcinomas of the lva, vagina urethra, and cervix. However lvar carcinoma is the only one in which e advantages of this form of treatment have en well demonstrated A decision regarding e others awaits further experience.

Squamous Cell Carcinoma of the Vulva

The microscopic control afforded by the emosurgical technic makes it possible to ex e vulvar carcinomas reliably and at the same ne, conservatively The technic is the same as ed elsewhere on the surface of the body The ial layer of fixed tissue usually separates eanly in four to six days (average 4.8 days)

Small lesions may be removed with no resulting defect or appreciable scar (Fig 140) Even more advanced lesions with extension into the vaginal and anal regions may be removed with surprisingly good final results (Fig 141) During removal of lesions which involve the region of the urethra an indwelling catheter is employed to prevent dilution of the fixative and soiling of the dressings (Fig 142) Cancers which extend deeply around the urethra are readily followed proximally with the catheter in place.

Therapeutic results in a consecutive series of thirty four cases of microscopically proved squamous cell carcinoma of the vulva were as follows There were sixteen cases listed as indeterminate because the patients died of inter



Fig 140 (A) Squamous cell carcinoma of the vulva, grade 2 malignancy It had recurred after removal by electrocautery (B) Healed lesion after chemosurgical excision. There was no recurrence after five years.

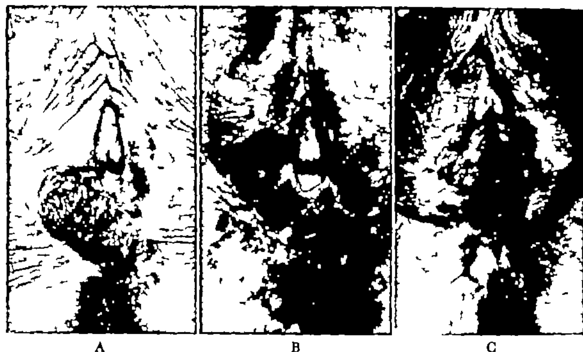


Fig 141 (A) Squamous cell carcinoma, grade 2 malignancy (B) Granulation tissue after chemosurgical excision. The cancer had invaded the vaginal wall and had extended to the anus. (C) Healed lesion. There was no recurrence when the patient died of other causes after two and one-half years.



Fig 142. (A) Squamous cell carcinoma, grade 1 malignancy (B) Granulation tissue after chemosurgical excision. The neoplasm involved the labia minora and majora bilaterally it extended up the posterior vaginal wall and it eroded the urethra. The indwelling catheter used during chemosurgical treatment is in place. (C) Healed lesion. There was no recurrence when the patient died of other causes after fifteen months.

disease but without carcinoma before
se of five years The remaining eighteen
inate cases included eight cases in which
nt was unsuccessful and ten cases in
the patients were free of carcinoma for
rs or more Therefore the five year rate
was 55 6 per cent

unsuccessful results in eight cases were
uncontrollable inguinal pelvic or other
ses. In two cases scattered metastatic
were present in the lymphatic vessels
external genitalia and groin these
conceivably might have been eradicated
ical vulvectomy but in these particular
he accompanying inguinal metastases
deep-seated that a groin dissection was
licated The factors which would be ex
to affect prognosis were the size of the
lesion previous unsuccessful treatment
tologic grade of malignancy the site of
and the presence or the absence of
sis.

*effect of the size of the lesion on the
cure* was considerable The smaller the
the better the prognosis thus both of
tients with group B lesions (1 to 2 cm
meter) were cured while six of nine
s (66 7 per cent) with group C lesions
3 cm) and two of seven patients (28.6
nt) with group D lesions (over 3 cm.)
ured The lower rate of cure in the groups
s with larger lesions was due to the higher
ce of metastases but it should be em-
ed that metastasis may occasionally occur
small vulvar lesions. In every case the
y lesion was eradicated regardless of the
the carcinoma.

effect of previous treatment on prognosis
rily would be expected to be adverse be
of the resultant delay with the increased
e of metastasis However in this series the
f cure was higher in the group of six
ts who had received previous surgical
iation treatment than it was in the group
lve patients who had not (66 7 per cent
50 0 per cent respectively) Undue sig
nce should not be attached to these
ics because the number of cases was
However the good results in the patients
previously had been treated unsuccessfully
ndicate the particular value of the chemo-
surgical method in cases of recurrent vulvar
carcinoma

The effect of the histologic grade of malignancy on the rate of cure was considerable Thus the five year rate of cure in the group of eleven patients with lesions of grade 2 was 63 6 per cent in the group of five patients with lesions of grade 3 malignancy the rate was 60 0 per cent while neither of the two patients with grade 4 lesions were cured There were no grade 1 lesions. The proportion of lesions with a high grade of malignancy was higher than elsewhere on the skin a fact which at least partially accounts for the lower rate of cure in series of vulvar carcinomas

The effect of the site of origin on prognosis appeared to be appreciable but the series was too small to allow definite conclusions to be drawn. The best end results were observed in patients with lesions of the labia majora (nine patients with a rate of cure of 77.8 per cent) while the prognosis was poorer in patients with lesions of the labia minora (four patients with a rate of cure of 50 0 per cent) and poorest in patients with carcinoma of the clitoris (four patients with no cures) These findings agree with those of most authors and are explainable on the basis of the relatively rich lymphatic drainage of the labia minora and especially of the clitoris One patient was successfully treated for a carcinoma which arose at the posterior fourchette.

The effect of metastases on the rate of cure was most definite All of the ten patients who did not have metastases were cured while none of the eight patients with metastases were cured. Only four of the patients with metastasis had regional nodes which were considered operable and in none of these was the result successful. Roentgen therapy to the inguinal metastases was given in five cases with fairly satisfactory palliation but no cures. In two cases roentgen therapy was given to enlarged inguinal nodes with permanent subsidence hence the enlargement was presumed to have been due to inflammation rather than to metastasis. In this series no prophylactic dissections of the regional nodes were carried out. However it should be emphasized that in view of the rich lymphatic drainage of the vulvar tissue, groin dissections should be considered an integral part

of treatment except in cases in which the primary lesion is small and the grade of malignancy is low In the latter group of patients it is justifiable to remove the primary lesion and then keep the patient under close observation for the usual five year period.

Comparison of the Therapeutic Results with Those of Other Authors

The five year cure rate of 55 6 per cent obtained with the chemosurgical technic compared favorably with the results of most authors The five year rates of cure obtained by several workers with the usual surgical technics are as follows Taussig,[88] forty-one selected cases in which Basset type operation was carried out, 58.5 per cent, Taussig, ninty five unselected cases, 48.5 per cent Bervan,[13] 407 cases, 41 per cent, McElvey[49] eighteen cases, 33.3 per cent Smith and Pollack,[87] 132 cases, 28 8 per cent Datnow[21] thirty five cases, 28.5 per cent and Palmer[73] 170 cases, 26.5 per cent. Taussig obtained superior results by the use of the Basset operation which consists of a vulvectomy bilateral groin dissection, and removal of iliac nodes plus removal of the intervening lymphatic bearing tissues.

Discussion

The excellent results attained with the Basset type of operation emphasize the importance of following the chemosurgical excision of the primary vulvar carcinoma with a groin dissection whenever the size and degree of malignancy of the primary lesion suggests any likelihood of metastasis. The groin dissection usually should be bilateral because of the richly anastomosing lymphatic drainage.

Since the spread of vulvar carcinoma to the groin is rarely by continuous permeation along the lymphatic vessels and since seeding of emboli along the vulvar lymphatics is uncommon, there is no need for vulvectomy in the majority of cases However in the occasional case in which there has been seeding along the lymphatics the Basset type of operation is advisable if both the primary and secondary lesions are operable Also in cases of severe senile atrophy or extensive leukoplakia vulvectomy may be the preferred method of eliminating the precancerous lesions. But in most cases the chemosurgical procedure is advantageous for two main reasons first, the removal of the primary lesion is more certain when carried out under microscopic control and second, the conservatism which may safely be practiced with the chemosurgical method is desirable especially in younger patients who are most interested in avoiding the disabling effects of vulvectomy on sexual function. The advantages of the microscopic control of excision are especially apparent when the carcinoma has invaded the vagina, clitoris, urethra or the perineum adjacent to the anus because in the presence of these irregular and often unpredictable extensions vulvectomy cannot be relied on to eradicate the primary lesion. However even when the primary lesion is relatively small the chemosurgical method often is more reliable because there may be slender clinically undetectable extensions which readily could be missed during vulvectomy but which may be accurately followed out by means of the microscopically controlled excisions which characterize the chemosurgical method.

In the presence of multiple nodules in the vulvar lymphatics the chemosurgical removal of the primary lesion might well be followed by radical vulvectomy in an attempt to eliminate the carcinoma in the lymphatics and in the regional nodes. This procedure would combine the greater reliability of the chemosurgical removal of the primary lesion with the efficacy of radical vulvectomy in combatting the metastatic foci. In the present series there were no cases suitable for this combined procedure but the author is convinced of the feasibility of this line of approach in selected cases.

Basal cell carcinoma of the vulva was chemosurgically excised in three cases. All of the lesions arose on the labia majora. One patient had two lesions both of which remained healed after seven years. The other two patients had presented no evidence of recurrence after three years when they died of unrelated causes.

Benign vulvar lesions also may be removed chemosurgically Examples of lesions which have been successfully treated by this method are squamous cell papilloma, leukoplakia, hemangioma, sebaceous cysts and radiation ulcer In the treatment of the last condition the necrotic and damaged tissues are removed to a

depth at which the vascularity is adequate for rapid epithelization (Fig. 191). For the other benign lesions the treatment usually consists of excision followed by cauterization with dichlor acetic acid unless the sections reveal a condition which requires deeper removal. In the latter event the zinc chloride fixative is applied and successive layers of tissue are removed as dictated by the microscopic findings.

Carcinoma of the Urethra

Thus far no primary urethral carcinomas have been removed chemosurgically. However experience with vulvar carcinomas which have invaded the urethra leads to the conclusion that urethral cancer should be amenable to chemosurgical treatment. This conclusion is strengthened by the fact that one urethral caruncle (capillary hemangioma type) was successfully removed by means of this method.

In the treatment of carcinoma of the urethra an indwelling catheter would be used during the period of active treatment. After surgical removal of the main mass under local anesthesia chemosurgical treatment would be instituted. The dressings would be held in place on the lesion by an externally placed dressing and by a perineal pad. At the completion of active treatment the dressings could be discontinued and the final layer of fixed tissue allowed to separate. The conservatism which could safely be practiced with the chemosurgical method would make possible the preservation of the sphincters unless these muscles were already extensively invaded by the cancer.

Carcinoma of the Vagina

No patients with carcinoma which could be considered to have arisen primarily in the vagina have been treated chemosurgically. However the fact that the chemosurgical technic is known to be feasible for carcinomas invading the vaginal wall from their site of origin on the vulva or on the prolapsed cervix indicates that the method also should be feasible for carcinomas originating in the wall of the vagina.

The technic would be the same as that used for lesions on the skin surface except that long handled instruments would be used and the dressings would be held in place by vaginal packing rather than by adhesive tapes. Upon completion of active chemosurgical treatment the dressings could be discontinued. As in vulvar lesions the final layer of fixed tissue would be ready to separate in four to six days.

Carcinoma of the Cervix

The advisability of using the chemosurgical method in the treatment of early carcinoma of the cervix has been considered. The usual combined roentgen and radium therapy fails to cure a small but significant number of patients with carcinomas supposedly localized to the cervix. The proportion of failures in the treatment of Stage I carcinoma varies from 20 to 50 per cent in the various reported series. If an appreciable proportion of these failures were due to radioresistance the chemosurgical method conceivably might be advantageous. Lynch[44] states that 20 per cent of cervical carcinomas are radioresistant but whether the failure to respond to radiation is mainly due to true biologic radioresistance or whether it is mainly due to extra-cervical spread which is unrecognized because of clinically undetectable extensions is not definitely known. Perhaps the only way to definitely determine whether or not chemosurgery should ever be used in the treatment of carcinoma of the cervix is to cautiously try the technic in cases in which radiation is contraindicated because of conditions such as inflammatory disease of the urinary or intestinal tracts, blood dyscrasias or possibly because of evidence of radioresistance as indicated by failure of the cervical lesion to respond promptly.

The technical feasibility of using the chemosurgical method for lesions of the cervix has been demonstrated during the successful removal of nabothian cysts, cervical polyps, cervical fibroids and cervical erosions. Five patients with the last condition were treated with prompt and permanent healing in all. The technic is similar to that used for lesions on the exterior surface of the body except that the dressings are kept in place by means of vaginal packing rather than by adhesive tapes. Long handled knives and forceps are necessary. The final layer of fixed tissue separates spontaneously in about four days and the wound heals rapidly without further attention.

CHAPTER 17

Carcinoma of the Anus and Lower Rectum

ALTHOUGH carcinomas of the anus and adjacent buttocks are amenable to chemosurgical treatment, carcinoma of the rectum usually should not be chemosurgically treated because of its tendency toward early metastasis to the intrapelvic lymph nodes.

Only a few carcinomas have been chemosurgically excised from the anal and surrounding tissues. One was a basal cell carcinoma which had arisen at the edge of the anus and had extended out on the buttocks and up the anterior wall of the anus and rectum despite treatment with radium. The rectal spread was not predicted by clinical examination prior to chemosurgical treatment and although it was found that the neoplasm skirted along the surface of the anal sphincter, this muscle was not affected enough to cause bowel incontinence. Two residual foci later were removed from adjacent areas and the patient apparently was free of carcinoma when she died of cardiac disease one year after the completion of treatment.

Four other patients with carcinoma of the anus were chemosurgically treated. Three of these had extensive squamous cell carcinomas which had metastasized to the inguinal lymph nodes. The infected foul smelling anal masses were removed as a palliative measure. A fourth patient had an adenocarcinoma in a cystic mass adjacent to the anus. During chemosurgical removal a tract was found which communicated with the lower rectum and it was thought that the carcinoma had arisen from rectal epithelium in a fistula. Due to involvement around the lower rectum the patient was referred for colostomy and resection of the rectum; after this procedure the patient remained well for at least six years.

These few cases are cited only to indicate that the chemosurgical technic is *applicable* to lesions in the vicinity of the anus. Infection never presented a problem because during chemosurgical treatment the fixative chemical sterilized the treated area while after separation of the final layer of fixed tissue the granulation tissue effectively resisted bacterial invasion. A colostomy was unnecessary. The patient was allowed to defecate after each layer of fixed tissue was excised. After the microscopic sections were examined the fixative and the dressing were reapplied and allowed to stay in place until the next excision. Upon completion of active chemosurgical treatment the dressing was omitted and a small amount of petrolatum was applied to the final layer of fixed tissue to prevent undue drying and shrinkage. The fixed tissue separated in approximately five days. The wounds healed rapidly even though the fecal material continually passed over the granulation tissue. In none of the cases was there sufficient stenosis to cause undue difficulty in defecation.

The exact role of chemosurgery in the treatment of anal carcinoma remains to be determined. It would seem that the method would have much to offer in patients with less advanced neoplasms than those treated up to the time of this writing. The microscopic control provided by the method should result in sure eradication of the primary lesion plus a degree of conservatism that often would allow preservation of the sphincter muscles. Furthermore, the procedure could be carried out without the necessity of a colostomy.

CHAPTER 18

Metastatic Cancer in Lymph Nodes

ALTHOUGH metastatic regional lymph nodes are almost always best removed by surgical means there occasionally may be in dications for chemosurgical treatment For ex ample if there is a localized but firmly fixed infiltrating metastatic mass in a region which is accessible enough for chemosurgical excision the microscopically guided excision afforded by this treatment might allow more certain re moval than would be possible surgically (Fig 120) However the technic cannot be used safely for the removal of nodes in the vicinity of the large vessels such as are present in the cervical, axillary and inguinal regions because damage to these vessels would lead to the com plications of thrombosis and hemorrhage Therefore even though part of the metastatic nodes occasionally may be removed chemo-surgically it may be necessary to have the rest of the chain dissected surgically (Fig 152)

In forty cases advanced fixed ulcerated regional nodes were chemosurgically excised for the purpose of palliation and although there was some temporary benefit the eventual out come was unsuccessful in most cases. It was concluded therefore that there was little justi fication for the procedure except in cases in which the neoplasm was sufficiently localized for there to be a reasonable chance of com-plete removal either by the chemosurgical technic alone or in combination with surgical dissection

The indications for surgical dissection of regional lymph nodes are discussed in the chapters on carcinoma of the skin lip vulva and other structures. In general dissection of nodes which are not palpably enlarged is not advised unless the primary lesion is fairly large and of a rather high degree of malignancy There are no set rules and a decision to advise a prophylactic dissection is made upon con sideration of these and other pertinent factors in each individual case In the presence of definitely enlarged regional nodes a surgical dissection ordinarily is indicated immediately unless there is considerable likelihood of the en-largement being the result of inflammation. In the latter event close observation for a week or two may be allowable but if there has not been rapid subsidence after that period the dissection should be carried out. If distant metastases are present or if the nodes are in-operable palliative roentgen therapy often is useful.

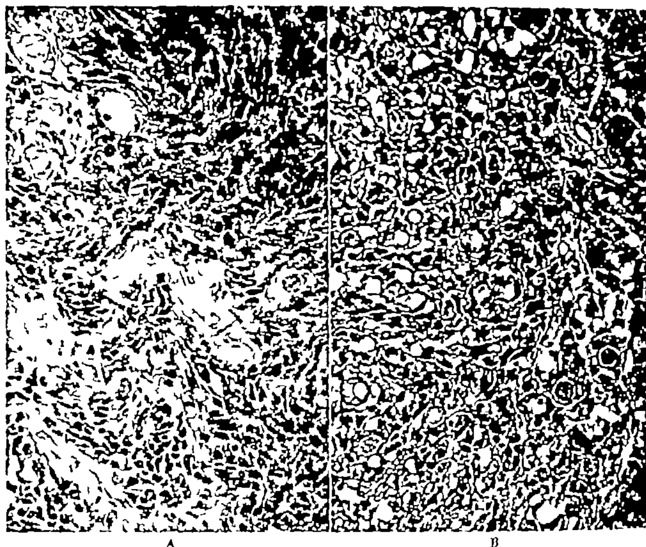


Fig 144 Photomicrographs of two melanomas with different degrees of malignancy and with correspondingly different outcomes. (A) Melanoma with a high degree of pleomorphism, with invasion of the thin-walled vessels and with extravasation of blood. The patient died of axillary and internal metastases although there was no recurrence of the primary lesion. (B) Melanoma with only moderate degree of pleomorphism, with intact vessel walls and no extravasation of blood. The patient whose lesion is illustrated in Figure 146 showed no evidence of melanoma after seven years.

Melanoma of the Skin

All but one of the melanomas which have been chemosurgically removed originated in the skin. Three-quarters of the cutaneous melanomas arose in nevi while the remaining one-quarter arose in skin which had appeared normal All of the patients were adults.

The importance of the removal of an extra zone of tissue at the periphery of a melanoma was demonstrated in the first case of this series (Fig 145) The neoplasm was chemosurgically excised to a level at which melanoma no longer appeared in the sections and then treatment was discontinued It was not until six weeks later that several satellite nodules became large enough to be seen and palpated. Fortunately a second chemosurgical excision which included a wide zone of apparently normal tissue at the periphery completely eradicated the neoplasm Thereafter it became routine practice to remove a generous amount of peripheral tissue whenever practical. As a result there have been no further cases in which the primary lesion was not controlled with one exception. In the last case the melanoma which arose on the eyelid was associated with scattered areas of junction nevus on the conjunctiva a new area of melanoma arose in the nevus and during removal of this new focus the patient suddenly died of coronary occlusion. In retrospect, the

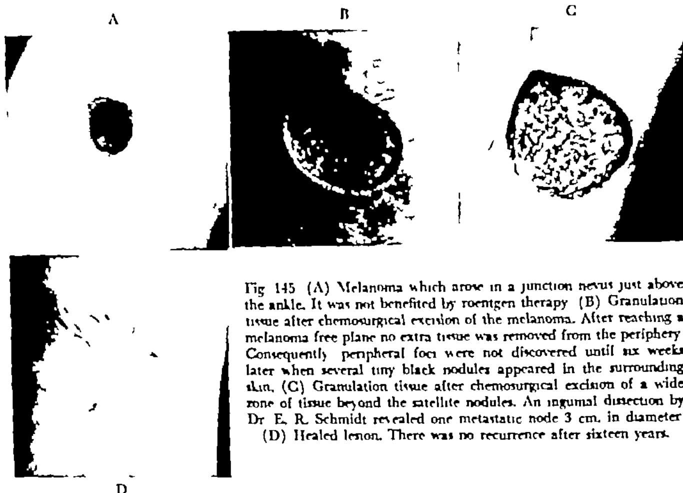


Fig 145 (A) Melanoma which arose in a junction nevus just above the ankle. It was not benefited by roentgen therapy (B) Granulation tissue after chemosurgical excision of the melanoma. After reaching a melanoma free plane no extra tissue was removed from the periphery Consequently peripheral foci were not discovered until six weeks later when several tiny black nodules appeared in the surrounding skin. (C) Granulation tissue after chemosurgical excision of a wide zone of tissue beyond the satellite nodules. An inguinal dissection by Dr E. R. Schmidt revealed one metastatic node 3 cm. in diameter (D) Healed lesion. There was no recurrence after sixteen years.

removal of the entire lower eyelid would have been preferable in this case because this would have eliminated the premelanomatous lesion.

Because of the dangerous propensity of melanoma to metastasize, there is justification for very radical treatment. However often it is desirable to be as conservative as safely possible in order to avoid excessive mutilation of the face (Fig. 146) or to avoid loss of function of an important part such as the hand (Fig 147) or the foot (Fig 148) The chemosurgical technic aids in the attainment of the maximal degree of conservatism consistent with reasonable certainty of complete eradication of the primary melanoma along with its satellite foci in the skin lymphatics.

Small melanomas in which there has been less opportunity for the formation of satellite foci, may be removed relatively conservatively (Fig 149) However if the small melanoma presents histologic evidence of high malignancy as indicated by marked pleomorphism, invasion of vessels and extravasation of blood its removal should be correspondingly wide (Fig 150)

Occasionally outlying areas of junction nevus may accompany melanoma and although there may be no visible connection with the nevus from which the melanoma developed, it is advisable to remove the entire affected area including the apparently normal intervening tissue (Fig 151)

Regional nodes ordinarily are not resected chemosurgically unless the primary and secondary deposits are so located that both can be removed in one piece (Fig 152) Usually surgical dissection of regional nodes is preferable

Therapeutic Results in Cases of Cutaneous Melanoma

Thirty-one adults with microscopically proved melanomas of the skin were chemosurgically treated during the twelve year period which ended six years prior to this writing The primary lesions varied widely in size but more than one half of the lesions exceeded 2 cm. in diameter Eighteen patients had received previous definitive treatment with radiation or some form of surgery including electrodes-

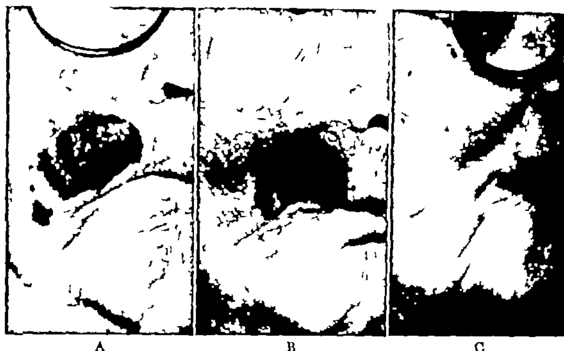


Fig 146. (A) Melanoma which had arisen in the medial half of a junction nevus and which had recurred after electrodesiccation. (B) Granulation tissue after chemosurgical excision of the melanoma and the nevus plus an extra zone 5 to 10 mm. at the periphery (C) Healed lesion. There was no recurrence when the patient died of an accident after seven years.

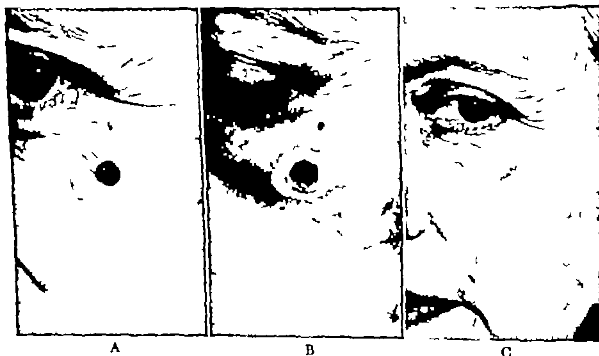


Fig 147 (A) Melanoma which had recurred after treatment with a caustic paste. (B) Granulation tissue after chemosurgical excision. (C) Healed lesion. There was no recurrence when the patient died of cerebral hemorrhage after six years.



A B C

Fig 148 (A) *Melanoma on the heel recurrent after treatment with caustics, electrosurgical excision and roentgen rays. (B) Granulation tissue after chemosurgical* excision. The enlarged inguinal nodes were surgically resected but exhibited only inflammatory hyperplasia (C) Healed lesion. The soft, pliable scar caused no discomfort on walking. There was no recurrence after ten years



A B C

Fig 149 (A) Melanoma which had arisen in a small junction nevus. (B) Lesion on the second day of the chemosurgical treatment. By the third day another 8 mm. had been removed from the periphery and two layers had been examined and found to be free of melanoma. (C) Healed lesion. There was no recurrence after six years.



Fig 150 (A) Melanoma which had arisen in the medial part of a junction nevus. (B) Granulation tissue after chemosurgical excision which was relatively wide because of marked pleomorphism, erosion of vessel walls and extravasation of blood in the neoplasm. (C) Healed lesion. There was no recurrence after six years.

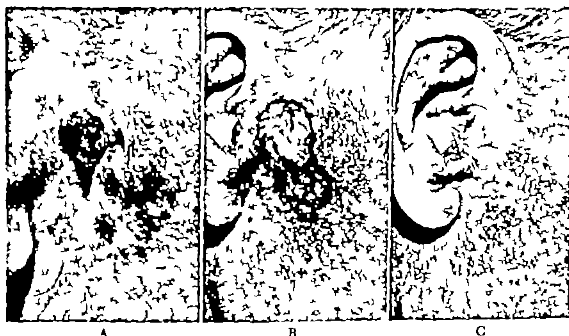


Fig 151 (A) Melanoma which arose in one of a group of junction nevi. (B) Granulation tissue after chemosurgical excision of the melanoma and all of the junction nevi along with the intervening normal tissue. (C) Healed lesion. There was no recurrence after ten years.



Fig 152 (A) Melanoma which had recurred under scars which had resulted from conservative surgical excision of the primary focus on the cheek and a metastasis in the preauricular node (B) Granulation tissue after chemosurgical excision of the primary and secondary foci. The latter had invaded the parotid gland but no facial paralysis was produced. Six months later a radical neck dissection by Dr E. R. Schmidt revealed metastases in the upper cervical region. (C) Healed lesion. There was no recurrence when the patient died of heart disease after nine years.

fication. Palpable enlargement of the regional lymph nodes was present in fourteen cases. All of the patients were followed for at least five years or until death.

Of the thirty-one patients in this consecutive series, twelve (38.7 per cent) were free of evidence of melanoma after five or more years (Table XLV) The patient who had remained well the longest was free of disease after sixteen years (Fig 145)

The causes of failure in the nineteen cases in which treatment was unsuccessful were uncontrolled metastasis in fourteen patients, coronary thrombosis during or shortly after treatment in two patients and death of indefinite causes before the elapse of five years in three patients. The last group is included in the "un successfully treated" category because the stroke" in one patient, the "pneumonia" in another and the undetermined cause of death" in the third all possibly could have been mani festations of metastatic melanoma

The effect of the size of the lesion on prog nosis is definite largely because of the greater likelihood of metastasis from melanomas of larger size. Thus the rate of cure varied from 80 per cent in the group with lesions under 1 cm in diameter to 25 per cent in the group with lesions over 3 cm. in diameter (Table XLVI) Stated differently for the group of

TABLE XLV

FIVE-YEAR END RESULTS FOR MELANOMA OF THE SKIN

This series includes the cases of all patients with histologically proved primary melanoma, both early and advanced, previously untreated and recurrent, with and without metastasis who were chemosurgically treated during the twelve year period ending six years prior to this writing

Total number of cases	31
Total number of determinate cases	31
Unsuccessful results, total number	19
Patients dead melanoma present at death	17
Patients lost from observation with melanoma	1
Patients living with melanoma	1
Successful results, patients free from melanoma for five years or more	12
Five-year rate of cure (12 ÷ 31) × 100	38 7%

TABLE XLVI

EFFECT OF SIZE OF MELANOMA OF THE SKIN ON FIVE-YEAR END RESULTS

Group	*Average Diameter Cm.*	*Number of Lesions*	*Successful Results Number*	*Per cent*
A	under 1	5	4	80
B	1 to 2	10	4	40
C	2 to 3	4	1	25
D	3 or more	12	3	25

fifteen patients with lesions under 2 cm. in diameter the rate of cure was over twice as high as for the group of sixteen patients with lesions over 2 cm. in diameter (53 3 per cent cf 25 per cent)

The effect of previous treatment on prognosis would be expected to be appreciable not only because of the delay occasioned by the unsuc cessful treatment but also because of the tendency of certain procedures particularly electrodesiccation, to cause melanoma to spread through blood vessels and lymphatics. In this series the rate of cure in the group of eighteen patients who had received previous treatment was 33 3 per cent as compared to the rate of 46.2 per cent in the group of thirteen patients who had not received previous treatment. The adverse effect of previous treatment on prog nosis was less than expected the fact that 33.3 per cent of the patients with recurrent lesions were cured emphasizes the value of the chemo-surgical technic in recurrent melanoma.

The effect of the histologic degree of malig nancy on prognosis is considerable Although melanomas always are considered highly dan gerous, their degree of malignancy is variable Histopathologic criteria have been observed to be of definite value in the estimation of prog nosis in the individual case.

The criteria used in the determination of the malignancy of melanoma were (1) pleo-morphism (2) invasion of vessel walls (3) extravasation of blood in the neoplasm and (4) pigmentation.

In this series of thirty-one cases there was a very high degree of pleomorphism in eighteen cases (58 per cent) The rate of cure in this group was only 33.3 per cent as compared to the rate of 41.9 per cent in the group of thirteen cases in which the degree of anaplasia was only moderately high.

Invasion of the walls of blood and lymph vessels was observed in 67 7 per cent of the cases. The rate of cure in this group of cases was only 13 3 per cent while in the group of ten cases in which there was no erosion of the vessels the rate of cure was 90 per cent.

Extravasation of blood in a melanoma is interpreted as an indication of erosion of the walls of blood vessels and hence is an unfavor able prognostic factor In this series the ra cure in the group of twelve cases in which t was extravasation was 38.7 per cent whi the group of nineteen cases in which there no extravasation the rate of cure was 42 1 cent.

Pigmentation was present in 67 7 per cen the melanomas Absence of pigment was an verse prognostic factor as indicated by a of cure of 33 3 per cent as compared to per cent in the group with pigmented lesion

In estimating the prognosis in a given c it has been observed that the greater the n ber of these unfavorable prognostic factors worse the prognosis. Thus, when none of t unfavorable factors were present the rate cure was 100 per cent, with one unfavor factor it was 50 per cent, with two it was per cent, with three it was 28 6 per cent with four it was 16 7 per cent.

The effect of site of origin on prognosis c not be evaluated adequately on the basis c series of thirty-one cases. However the num of cases and the rate of cure for each anato site were recorded as follows head and ne sixteen cases with 43 8 per cent cure up extremities, two cases with 50 per cent cu trunk, two cases with no cures lower tremities eleven cases with 36 4 per cent cu Ordinarily it would be expected that m tastasis and unfavorable results would be m likely in areas most subject to trauma a motion.

The effect of metastasis on prognosis is m striking In the group of twenty patients w at some time developed regional or dist metastases the rate of cure was 10 per c while in the group of eleven patients witho metastases the rate of cure was 90 9 per ce Thus in presence of metastasis the progno is grave though not hopeless, while in t absence of metastasis the prognosis is excelle

In only seven patients were the metasta definitely recognized at the initial visit. In th group successful results were obtained in o case (14.3 per cent cure) Contrastingly, in t group of twenty four patients in whom m tastases were not initially apparent there we eleven successful results (45 8 per cent cure)

Other factors which were considered to be

possible prognostic significance were the duration of melanoma the rapidity of its growth and the presence of ulceration. However, the only one of these factors which had any appreciable bearing on the prognosis in the cases of this series was ulceration Thus, in the group of twenty-one cases in which ulceration was present *the rate of cure* was *only* 33.3 *per* cent as compared to 50 per cent in the ten cases in which ulceration was absent

Melanoma of Other Tissues

Melanoma of tissues other than the skin is relatively rare The only case which has been observed in the Chemosurgery Clinic was that of a patient with a melanoma which arose on the mucosa of the nasal septum. This was chemosurgically excised and there was no evidence *of recurrence until after six years when* a new focus suddenly appeared high on the septum. This recurrent mass was found to extend to the ethmoid region but it was excised chemosurgically by an approach through the naris. There was no evidence of recurrence two years later or after a total of eight years after the initial treatment. This result is noteworthy because among the total of sixty two cases of melanoma of the nasal mucosa which have been reported in the literature there was only *one other patient who survived longer than* two years.[33]

No intraocular melanomas have been chemosurgically treated at this writing but in cases in which there *has been extraocular extension* the chemosurgical technic probably would offer a better chance of complete eradication than would the usual surgical enucleation or exenteration of the orbit. Postoperative recurrences also might constitute indications for chemosurgical treatment

Juvenile Melanoma

Juvenile melanoma usually is a relatively benign disease and hence such lesions were excluded from the series of melanomas in adults. One juvenile melanoma was chemosurgically excised from a child three years of age, and there was no evidence of recurrence after five years.

Comment

A major advantage of the chemosurgical treatment of melanoma is the reliability which is attested by the five year rate of cure of 38 7 per cent. This rate is the same as the best rate obtained with radical surgery (Table XLVII) The reliability of the method is further indicated by the fact that the primary lesion apparently was eradicated in thirty of thirty one cases (96 8 per cent) The low rate of recurrence of the primary lesion (3.2 per cent) *compares favorably with the rates given by* other authors as for example 28 3 per cent by Pack[14] and 30 per cent by Farrell[illegible]

TABLE XLVII

COMPARISON OF THE FIVE-YEAR END RESULTS OF CHEMOSURGICAL TREATMENT OF CUTANEOUS MELANOMA WITH THE END RESULTS OF OTHER AUTHORS

Author	*Treatment*	*Number of Determinate Cases*	*Successful Results Number*	*Successful Results Per cent*
Mohs	Chemosurgery	31	12	38 7
Scharnagel[illegible]	Surgery and radiation	49	19	38 7
Ackerman	Surgery †	21	8	38 0
Cholnoky[14]	Surgery	26	9	34 6
Pack *et al*[73]	Surgery §	70	23	33 0
Pack *et al*[7]	Surgery ‡	575	123	21 4
DeWeese[illegible]	Surgery	62	16	25 4
Taussig and Torrey[24]	Surgery	35	7	20 0
Deland and Holmes[15]	Surgery	82	15	18 3
Affleck[3]	Surgery	1?0	4	2 3

Compilation of results at Radiumhemmet, Stockholm.

† *This group was limited to cases in which radical* excision and lymph node dissection were done In the entire group of forty-three treated cases the survival rate was 19 per cent.

‡ *Pack s series included* a number of cases that would be considered inoperable by many surgeons.

§ Previously untreated patients only

The high rate of cure stems from several factors. First, the microscopic control assures removal of the primary melanoma including any silent outgrowths that not infrequently are present. Second, the melanoma is never cut into, even for the purpose of biopsy until the tissue has been fixed chemically thus reduces the chance of dissemination through the blood or lymph streams. Third the removal of a zone of peripheral tissue as wide as indicated by the microscopic findings in the individual neoplasm reduces the chance of recurrence from deposits in the peritumoral lymphatics.

A second major advantage of the chemosurgical treatment of melanoma is that the method often makes it possible to avoid excessively mutilating operations. This conservatism in part is due to the microscopic control of excision which assures complete removal of the primary lesion without the sacrifice of large amounts of uninvolved tissue. It also is partly due to the fact that the histologic studies make it possible to estimate the distance to which the satellite deposits would be likely to have spread and thus to judiciously limit the width of the excised safety zone. The fact that thirty of thirty-one primary lesions apparently were eradicated by this procedure indicates its adequacy

A third major advantage is the safety with which a chemosurgical biopsy may be taken in cases in which the diagnosis is questionable. Some cases of pigmented basal cell carcinoma, seborrheic keratosis (Fig 188) pigmented nevus basal cell carcinoma arising in an intradermal nevus, ulcerated hemangioma histiocytoma dermatofibroma pyogenic granuloma (Fig 186) and other conditions may be difficult to differentiate clinically from melanoma When there is some doubt it is safe to remove the lesions conservatively by the chemosurgical technic. Then if the lesion proves to be relatively benign the excision may be correspondingly conservative. However, if the lesion proves to be melanoma the excision may be carried forward to an appropriately radical level. There is evidence that the inflammatory process produced by the fixative chemical tends to limit dissemination of neoplastic cells, possibly by the same mechanisms as those which operate to limit the spread of invading microorganisms from an inflamed area. Hence there is no danger of disseminating melanoma during the layer-by layer chemosurgical excision.

A fourth major advantage of the chemosurgical method for the excision of melanoma is the very low operative risk. In the present series there were only two deaths during the period of chemosurgical treatment. Both were the result of coronary occlusion and there was no evidence that the chemosurgery had anything to do with the onset of this cardiac complication.

The great variation in the degree of malignancy and in the behavior of melanoma often is overlooked. Some patients with large primary lesions and one or two metastases in the regional nodes still may be curable. On the other hand some patients with small primary lesions and no perceptible metastases may have far flung deposits which may become evident several months or years later Because of this variability of the disease it is essential that treatment be prompt, vigorous and persistent until the melanoma either has been eradicated or has become too disseminated for any hope of cure

CHAPTER 20

Sarcoma and Endothelioma

IN the treatment of sarcoma and endothelioma the microscopic control of excision afforded by the chemosurgical technic is just as advantageous as it is in the treatment of carcinoma.

Sarcoma

Many external sarcomas are invasive infiltrating neoplasms which send out slender strands and thin sheets into the surrounding tissues. Since these extensions are difficult to detect clinically or grossly at operation their recognition and eradication are best assured by microscopically guided chemosurgical excision.

The chemosurgical technic is essentially the same as used in the treatment of carcinoma. However with certain types of sarcomas the interpretation of the microscopic sections may be somewhat more difficult for the inexperienced operator who may confuse the neoplastic cells at the periphery with normal cells.

In the treatment of sarcomas in the various anatomic sites the problems and the final results are similar to those encountered with carcinoma in the same areas. Thus, in a case of sarcoma of the lip the treatment and the outcome was the same as in carcinoma of the same organ (Fig 153) Cutaneous lesions of moderate size were removed without difficulty (Fig 154) Sarcomas of large size were successfully removed from the areas not adjacent to vital structures as for example, those located on the back (Fig 155) and on the buttocks (Fig 156) However insuperable difficulties were



Fig. 153 (A) Spindle cell sarcoma. (B) Healed lesion after chemosurgical excision. There was no recurrence after five years.



Fig 154 (A) Fibrosarcoma which had recurred after surgical excision. (B) Granulation tissue after chemosurgical excision. (C) Healed lesion. There was no recurrence after five years.



Fig 155 (A) Two rapidly-growing fibrosarcomas of the dermatofibrosarcoma protuberans type which arose amidst slowly-growing multiple fibromas which had been present on the back for twelve years. (B) Granulation tissue after chemosurgical excision of the sarcomas and the fibromas. (C) Healed lesion. No grafts were used but the resultant scar was soft, smooth and asymptomatic. There was no recurrence when the patient died of other causes after fifteen years.

encountered in cases in which the neoplasm was found to invade vital structures such as the large vessels of the neck, the brain or the spinal cord (Fig 157)

Although undifferentiated types of sarcoma often have a serious prognosis and often require radical removal and dissection of the regional nodes, the less malignant forms such as fibrosarcomas, myxosarcomas and liposarcomas can be treated less drastically without excessive risk.





A B C

Fig 156. (A) Neurofibrosarcoma in an eighteen month old child with a bathing trunk type of nevus. (B) Fixed tissue at completion of chemosurgical excision. (C) Healed lesion. There was no recurrence after seven years.





A B C

Fig 157 (A) Fibrosarcoma in a girl, age twenty-three. The neoplasm had recurred after three surgical excisions and had not responded to roentgen therapy (B) Granulation tissue after chemosurgical excision of most of the highly vascular sarcoma. Aplastic anemia was a temporary complication of treatment. Several eroded vertebral spines were removed but the sarcoma was found to have invaded into the spinal canal. Therefore treatment was discontinued. (C) Lesion after split-thickness grafts had been placed by Dr J W Gale The patient was much improved for a year but the disease caused the patient's death after two years.

An example is a case of lipomyxosarcoma of the thigh. The neoplasm had recurred after surgical excision during which fragments of sarcoma tissue apparently were disseminated over a wide area. A number of foci were chemosurgically removed as they became manifest, and two years after the last treatment the neoplasm appeared to have been brought under control without resort to amputation or inguinal dissection. The decision to pursue this conservative

course was based on the histologic evidence that the tumor was of relatively low malignancy and that it would not be likely to metastasize.

While most of the neoplasms arose in the more superficial tissues such as the dermis, subcutaneous connective tissue or fascia several were of deeper origin. For example a synovial sarcoma (also called synovial endothelioma or synovioma) which arose in the capsule of one of the tarsal joints was removed despite rather extensive invasion between the tarsal bones (Fig 158) There was no recurrence of the primary lesion after three years, but pulmonary and vertebral infiltrations developed presumably due to metastasis.

Lymphosarcoma in some cases appears to originate as a single focus although more often there are multiple foci from the beginning When the lesions are multiple, roentgen therapy is employed to shrink down the tumors which are highly radiosensitive though not often radiocurable. However if there appears to be a single primary lesion in an accessible region chemosurgical treatment with its microscopic control provides the best chance of complete eradication of the disease. In certain circumstances the chemosurgical removal of as much as possible of the lymphomatous mass prior to radiation treatment may be indicated. For example, in one patient with a reticulum cell



Fig 158 (A) Synovial sarcoma which apparently originated in the articular capsule of one of the tarsal joints. The tumor had recurred after two attempts at surgical excision. (B) Exposed tarsal bones after chemosurgical excision. The neoplasm not only extended for an unexpectedly great distance at the proximal and distal edges but there was invasion into the third cuneiform bone and into the joint space between the second and third cuneiforms and the navicular bone. One extension was within a tendon sheath. (C) Healed lesion. The patient walked without a limp. There was no recurrence of the primary lesion after two years but spinal and pulmonary infiltrations which were assumed to be metastases had appeared.

sarcoma which nearly buried three of the anterior upper teeth the ulcerated mass along with one floating tooth was chemosurgically excised. Then when the sections revealed the highly malignant unencapsulated nature of the neoplasm and when roentgenograms revealed extension for four centimeters into the palatine process of the maxilla 1000 kV roentgen therapy was instituted by Dr E. A Pohle with elimination of symptoms up to the time of writing which is two and one-half years later Occasionally benign lymphoid lesions must be differentiated from malignant lymphomas. An example was the case of a patient with a benign lymphocytoma on the tip of the nose this lesion was chemosurgically excised and there was no recurrence after five years.

Therapeutic results in a consecutive series of cases of sarcoma were as follows There were twenty cases in the series, but two patients were lost from observation without recurrence before the lapse of five years. Thus, there were eighteen determinate cases Successful results were obtained in ten of these. Therefore, the five year rate of cure was 55.5 per cent.

The factors which may influence the rate of cure are the size of the lesion previous treatment, histologic type, site of origin and metastasis.

The size of the lesions exceeded 3 cm. in diameter in all but one case. The rate of cure for the lesions over 3 cm. in diameter was 52.9 per cent. The one smaller lesion was cured.

Previous unsuccessful treatment by means of surgery or irradiation was associated with a reduced rate of cure. Thus, the rate of cure for the group of fourteen patients who had received previous treatment was 50 per cent while the rate for the four patients who had not been treated previously was 75 per cent. The time which elapsed while the unsuccessful treatment was being received had a tendency to allow the sarcomas to spread to invo structures or to metastasize with the r adverse effect on prognosis.

The histologic type of sarcoma also the rate of cure. The relatively low de malignancy exhibited by dermatofibro protuberans was reflected in the 100 p rate of cure in the group of three cas large lesions of this type (eg Fig 15 next highest rate of cure was 54.5 per the group of eleven cases of fibrosarc other types (eg Figs. 153 154, 156 an The lowest rate of cure was 25 per cen group of four cases of undifferentiated s The more highly malignant neoplasms latter group were designated as spind round cell and polymorphous cell sarcor they exhibited a strong tendency to inva structures and to metastasize.

The site of origin of the sarcomas ha effect on the curability Some sarcoma not be eradicated because of invasion brain, spinal cord or large vessels of t or axilla. However the group of cases small to draw valid conclusions regard relative curability of sarcomas in regions.

Metastasis strongly affected the rate of patients with sarcoma. Thus, in th of six patients who had regional metast rate of cure was only 16 7 per cent s pared to the rate of 75 per cent in the g twelve patients who had no metastases.

Endothelioma

One patient with hemangioendothelio chemosurgically treated. The large fu mass affected over half of the anterior of the lower leg. As is usually the ca was no metastasis even though the p lesion was large. The patient remain after more than ten years.

CHAPTER 21

Modes of Spread of Cancer

IN the preceding chapters which dealt with cancer in the various accessible regions of the body there were cited many instances of clinically unpredicted outgrowths from the main neoplastic mass. In some cases these "silent" extensions were confined largely to one type of tissue such as the dermis, fascial planes, periosteum perichondrium embryologic fusion planes nerve sheaths, lymphatic vessels or blood vessels. In other cases the neoplasms exhibited no specific preference for any particular tissue but nevertheless irregular outgrowths were formed, apparently as a result of the countless local variations in the mechanical and nutritive conditions which affect the spread of cancer [69]

An appreciation of the fact that these slender strands or thin sheets of cancer often may extend for some distance from the clinically visible or palpable mass is essential to all who have to do with the treatment of neoplastic disease. In this chapter certain patterns of neoplastic spread are described and illustrated by means of photographs, photomicrographs, diagrams and reconstructions. These will indicate how cancers of a certain type located in a certain area will tend to act, but it is to be emphasized that each cancer has its own individual behavior pattern which cannot be fully delineated except by systematic microscopic examination such as may be accomplished by means of the chemosurgical technic.

Besides being of interest to the practical cancer therapist, some of the newly-described phenomena are of interest to the oncologist who is concerned with the mechanisms by which neoplasms invade normal tissues. Of particular interest is the fact that besides the well known quantitative variation in the degree of invasiveness of different cancers, there also is a qualitative variation in invasiveness whereby one cancer may have an affinity for one type of tissue while another cancer possibly of the same histologic type, may have an affinity for a different tissue.

Cancers with Affinity for the Dermis

The most common specific tissue affinity exhibited by cancer of the skin is for the dermis. The majority of the more highly invasive basal cell carcinomas show some degree of predilection for this tissue the predilection is considerably less commonly observed in less invasive basal cell carcinomas and in squamous cell carcinomas. Carcinomas with a strong tendency to spread in the dermis occur most commonly in the upper part of the face, namely the forehead (Fig 6) the temples (Fig 4) and the scalp (Fig. 5) but they also are common on the neck (Fig 37) nose and other parts of the face. Basal cell carcinomas of the trunk rarely exhibit affinity for the dermis in fact the dense dermis of the back actually acts as a barrier to the deep spread of these neoplasms.

Cancers with a strong affinity for the dermis may be found to radiate intradermal outgrowths for several millimeters or even centimeters from the main mass while their spread into the deeper tissues may be minimal. Since the intradermal spread tends to consist of slender interspersing strands, the initial stages of this invasion are not clinically detectable by gross visualization and palpation. In time however the intradermal involvement of a given area becomes sufficiently thick to produce clinical signs, such as palpable induration, visible pearly tissue and ulceration, but by this time

the clinically undetectable peripheral involvement has swept beyond

The tendency to send silent outgrowths into the dermis is most striking in more advanced lesions where the unexpected involvement may extend for many centimeters from the grossly visible portion (Fig 11) However the phenomenon also may be observed in fairly early lesions though in lesser degrees (Fig 4) Since the clinically undetectable zone tends to be wider around large lesions than around small ones, it follows that treatment whether by surgical excision or by radiation therapy should include a wider zone around large lesions than around small ones. With chemosurgical treatment, of course, excision is limited to the microscopically demonstrated limits of invasion and no extra tissue need be removed.

The width of the zone of silent intradermal invasion may vary at different points at the periphery of the cancer In some cases extension may be several times as great on one side as it is on the other sides (Fig 5) and in such instances the advantage of microscopically guided excision is particularly great.

Squamous cell carcinoma occasionally may show some degree of intradermal spread (Fig 18), but usually the phenomenon is much less striking than in highly invasive basal cell carcinoma However two instances of extensive invasion of the dermis of the skin of the lower lip and chin from a squamous cell carcinoma of the vermilion border of the lower lip have been observed Occasional instances of striking submucosal spread from a carcinoma of the lip also have been observed (Fig 113)

Cancers with Affinity for Fascial Planes

Many cancers show a tendency to invade down to the fascia and then spread peripherally in or on the surface of this tissue. For example, in one case the cancer arose in the skin over the dorsum of the second metacarpophalangeal joint and extended around to the palmar side of this structure. On clinical examination it seemed almost certain that the cancer extended through the joint (Fig 159A) However upon chemosurgical removal it was found that the cancer had followed the surface of the fascia around the joint which accordingly was not damaged (Fig 159B and C)

Other examples may be cited Cancer in the

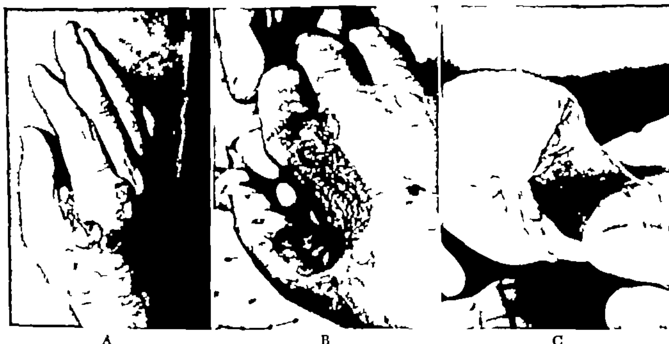


Fig 159 (A) Squamous cell carcinoma which had recurred after electrosurgical excision The mass extended around the metacarpophalangeal joint and appeared to extend into it (B and C) Granulation tissue after chemosurgical excision The cancer followed the surface of the fascia but did not penetrate it hence the joint was spared There was no recurrence after five years.

temporal region has been observed in many cases to invade to the *temporalis fascia* and then to spread peripherally often with extension inferiorly beneath the zygomatic arch, to the tendinous insertion on the mandible—all without invasion of the underlying temporalis muscle (Fig 23) In a case of basal cell carcinoma of the buttocks the neoplasm extended upward in the fascial planes on the inner and outer sides of the external anal sphincter but spared the structure and function of the muscle itself In a case of squamous cell carcinoma of the parotid gland a deep extension followed anteriorly along the fascia and epimysium of the stylohyoid muscle for an unexpected distance (Fig 125) Such an extension would have been a sure source of recurrence if it had not been followed out with the microscopic *guidance provided by the chemosurgical technic*. In several cases cancer overlying the sternocleidomastoid muscle has been observed to follow along the fascia around the anterior edge of the muscle (Figs. 33 and 34) and in one case it extended around the posterior edge (Fig 35) Apparently the resistance to the spread of cancer is less in or on the fascia than it is in the underlying muscle. Many carcinomas of the lower lip are observed to extend more deeply on the anterior or posterior surfaces of the orbicularis oris muscle than they do into the muscle itself

An appreciation of the fact that cancer frequently spreads along fascial planes and spares the underlying tissues, for a time at least, is often instrumental in the preservation of useful structures.

Cancers with Affinity for Periosteum

Some cancers invade to the periosteum and then spread peripherally along this tissue. This phenomenon is most frequently observed in the "fixed" areas of the face where the skin closely overlies the underlying bone as on the temple the malar eminence, the external auditory canal, the upper *half* of the nose and in the inner and outer canthal regions

Numerous striking examples of the tendency of some cancers to follow periosteum have been observed. In the inner canthal region basal cell carcinomas which have become rather advanced usually show a strong tendency to extend posteriorly *along the periostum of the medial wall* of the orbit (Fig 84) Since the extension tends to be localized largely in the region of the periosteum, it usually is unnecessary to damage the eyeball or the extraocular muscles during chemosurgical removal of the cancer The same phenomenon occasionally may be observed in lesions at the outer canthus (Fig 96) and at other points on the orbital rim.

In some cases the periosteal involvement is out of all proportion to the clinically detectable portion of the neoplasm. In a case of squamous cell carcinoma of the external auditory canal the neoplasm appeared to be localized to the lower half of the ear but upon chemosurgical excision it was determined that there was a sheet of cancer in the periosteum of the temporal, *parietal and occipital bones, extending* fully 10 cm. from the visible and palpable mass. In addition the periosteum of the bony canal, the middle ear and the canal of the Eustachian tube also was involved.

In another case, a recurrent basal cell carcinoma of long duration appeared to be largely localized to the temple, though there was some indefinite palpable thickening over the inferior rim of the orbit. Upon chemosurgical excision the cancer was found to have invaded along the periosteum over much of the floor of the orbit, the roof of the antrum, and the nasal bone. In the orbit and antrum the thickness of the layer of cancer was nearly 1 cm., but in the more recently involved periosteum of the nasal bone the thickness was only 1 mm. In this, as in many other cases, the invasion of the periosteum was impossible to detect by palpation until the cancer had grown thick enough to cause gross irregularity in the outline of the bone.

Cancer with Affinity for Perichondrium

Carcinomas overlying the cartilages of the nose or ear sometimes are observed to invade *to the perichondrium and then spread* out in this tissue or in the immediately overlying connective tissue. Owing to the thinness of the cutaneous and subcutaneous tissues of the ear all but the very early cancers extend to the perichondrium, and not infrequently they

spread out more widely on the surface of the cartilage than they do in the more superficial tissues (Figs. 68 69 and 91) The cartilage itself like bone constitutes a barrier to the further spread of cancer and it is only in the more advanced lesions that this tissue is penetrated. Carcinomas arising in adjacent structures such as the parotid gland may invade to the ear and then follow the perichondrium (Fig 124)

However, since the strands of cancer invading this tissue often are very small in caliber they often are not detectable by clinical examination (Fig 160)

Cancers with Affinity for Embryologic Fusion Planes

Carcinomas which overlie embryologic fusion planes may invade to an unexpected depth owing apparently to the disposition of the

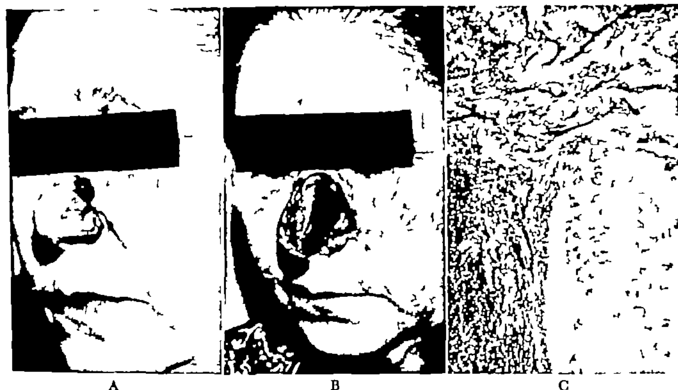


Fig. 160 (A) Basal cell carcinoma which had recurred after roentgen therapy (B) Granulation tissue after chemosurgical excision of the cancer which extended through the ala and bridge. The furthest peripheral spread was in the perichondrium and the adjacent tissues. (C) Photomicrograph showing the dark-staining cancer cells in the form of slender strands which are interspersed among the perichondrial and adjacent tissues.

Cancer of the nose as it invades the vicinity of the nasal cartilages may be deflected along the perichondrium producing a neoplasm of very irregular shape This irregularity plus the circumstance of the similarity between the consistency of cancer and that of the tissues of the nose accounts for some of the failures to eradicate the more advanced nasal carcinomas by ordinary surgical and radiologic methods.

The degree of specific affinity for perichondrium usually is not great rarely does the cancer extend for more than 5 or 6 mm beyond the advancing edge in the adjacent tissues.

planes of connective tissue and the tissue spaces in a direction perpendicular to the surface of the skin in these zones.

The most frequently observed lesion showing spread along a fusion plane is the common basal cell carcinoma of the nasolabial fold area (Figs 20 and 59) Neoplasms arising in this region and on the nasal ala often present a particularly troublesome therapeutic problem for several reasons first they often are highly invasive second, they are difficult to outline by palpation because of the similarity of the consistency of cancer and the fibrocartilaginous

tissue of the nose and, third, there is the strong tendency for the deeper lesions to invade the embroyologic fusion plane The direction of this invasion is in a plane which lies perpendicular to the skin of the cheek (*Fig 161*) Another place in which certain cancers invade particu

to be an inherent characteristic of the individu cancer Thus two neoplasms of the same hist logic type and with equal access to the san nerves may behave dissimilarly with one havir *a strong tendency to follow* the nerves and th other having absolutely no such tendency



Fig 161 (A) Basal cell carcinoma, which had recurred after x ray and radium treatment. (B) *Granulation tissue after chemosurgical excision, showing the depth* of extension into the embryologic fusion plane (arrow) Insert shows a reconstruc tion of the cancer The photograph, which was taken from above, shows the shape of the extension into the fusion plane (arrow)

larly deeply is the fusion plane in the midline of the lower lip and chin (Fig 32)

Cancers with Affinity for Nerve Sheaths

Some neoplasms exhibit a striking tendency to send out extensions in the nerve sheaths. In some cases one or more nerves may be selec tively followed for several centimeters (*Fig* 162) Usually the cancer is in the form of a cylinder several cells thick surrounding the nerve just beneath the perineurium (Fig 162E) near the point of exit from the main mass of cancer however there also may be in volvement of the epineurium and endoneurium (Fig 162D)

The selective affinity for nerve sheaths seems

The affinity for nerve sheaths exhibited by some skin cancers is such a striking phenomenon that it is surprising that no mention of it can be found in the literature. Of course the spread *of carcinoma of the prostate in the perineural* lymphatics is well known[44] and there have been references to the perineural spread of cancer of the lip[21] and of the salivary glands.[23] Probably the chief reason why the perineural spread of cancer of the skin has not been observed previously is that prior to the development of chemosurgery there was no convenient way to make a systematic study of the microscopic features of the periphery of these neoplasms.

Despite the fact that the extension of cancer

of the skin along nerve sheaths is a previously unreported phenomenon it is not rare In the present series the incidence of selective affinity for the perineurium was 2.4 per cent for squamous cell carcinoma (41 of 1,731 cases)

In one case the cancer traversed the sheaths of many nerves one of which it followed to the mental foramen in the mandible (Fig 163) In other cases the carcinoma was found to have entered the mental foramen and to have ex-

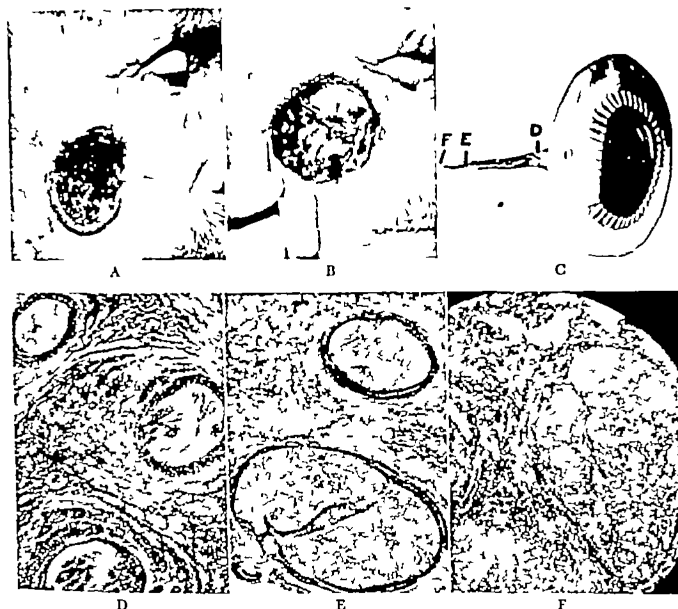


Fig. 162. (A) Squamous cell carcinoma which had recurred after radium treatment. There was some paralysis of the lower eyelid (B) Granulation tissue after chemosurgical excision. An applicator is inserted in the sinus tract which was tunneled out while following an involved nerve into the parotid gland. (C) Reconstruction of the tumor showing the cancer which extended for 5 cm. along a branch of the facial nerve (D) Photomicrograph taken near the main mass (point D on the reconstruction) (E) Photomicrograph taken near the *termination of the cancer in the parotid region showing exclusive localization* in the perineurium (point E on the reconstruction) (F) Photomicrograph of the same nerves in the middle of the parotid gland just beyond the farthest extension of the cancer

and 0.92 per cent for basal cell carcinoma (23 of 2 483 cases)

The incidence of selective affinity for nerve sheaths exhibited by squamous cell carcinoma of the lip was 2.3 per cent (15 of 642 cases)

tended along the inferior dental canal One carcinoma which had metastasized from the lip to the submaxillary region extended for several centimeters along the buccinator and facial nerves the latter nerve was followed into the

stylomastoid foramen hence the complete removal of the neoplasm was not feasible.

The highest incidence of spread along nerve sheaths was 18.2 per cent (six of thirty three cases) which was exhibited by carcinoma of the parotid gland. Whether this is because those neoplasms have access to many large nerves (facial great auricular auriculotemporal and sympathetics) or whether it is because of an inherent affinity of many of these neoplasms for nerve sheaths is not certain. Probably both of the parotid gland itself but cancers invading the parotid gland from the overlying skin often exhibit affinity for the nerve sheaths (Fig. 23)

Because nerves are omnipresent, cancers of almost any area might be expected occasionally to invade along nerve sheaths. One carcinoma of the penis invaded for some distance in the perineurium (Fig 137) Three sarcomas also exhibited some degree of selective affinity for nerve sheaths.

It should be pointed out that this series in-

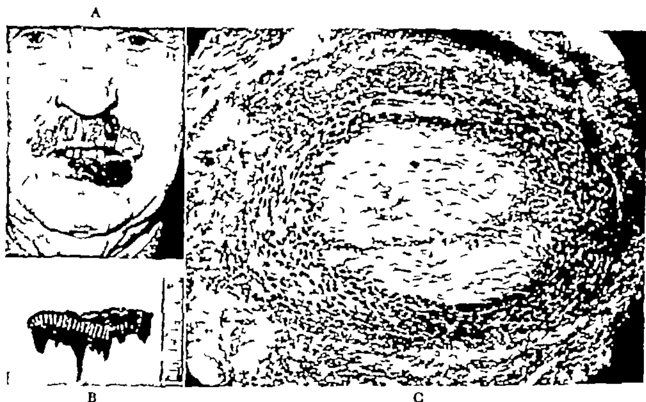


Fig. 163 (A) Squamous cell carcinoma, grade 2 malignancy (B) Reconstruction of cancer showing pincushion appearance owing to multiple extensions along nerve sheaths. The longest extension ended at the mental foramen. (C) Photomicrograph of cancer in nerve sheath near mental foramen.

factors are operative. At any rate, when the nerve sheaths are involved the microscopic control attained with the chemosurgical technic is invaluable in assuring complete extirpation of the cancer because without this control it is impossible to determine, either clinically or by gross examination at operation, whether or not the nerve sheaths are invaded. In some cases the nerves are followed selectively for a long distance in one case the carcinoma extended from the preauricular portion of the parotid gland to the rim of the orbit in the sheath of a branch of the facial nerve Not only carcinomas cluded an unusually high proportion of advanced lesions, and in fully a third of the cases there had been recurrence after previous radiation or surgical treatment elsewhere. Of the patients with squamous cell carcinomas of the skin which showed selective affinity for nerve sheaths 61 per cent had received previous surgical or radiation treatment, while of those with basal cell carcinoma twenty two of twenty-three had received previous treatment. Whether previous treatment enhanced the likelihood of perineural invasion or whether perineural spread was inherently associated with the more

troublesome, recurrent lesions has not been demonstrated but the latter seems most likely. The squamous cell carcinomas with affinity for nerve sheaths had a higher than average malignancy as indicated by the following figures: grade 1, no cases; grade 2, 36.6 per cent; grade 3, 53.7 per cent; grade 4, 9.7 per cent. All of the basal cell carcinomas with spread along nerves were classified as "highly invasive" and many of the lesions showed signs of increasing malignancy, anaplasia and metaplasia such as are often observed following repeated unsuccessful treatment with x rays and radium.

From the information now available it is uncertain whether the tendency of certain cancers to follow nerves is due to mechanical factors or whether it is due to nutritional factors; probably both are involved. That the cleavage plane between a nerve and its sheath provides a path of decreased resistance is indicated by injection experiments in which dyes and radiopaque materials were observed to follow the perineurium for considerable distance.[81,82] On the other hand, it is well established that nerves require adequate nutrition along their entire lengths and that this is assured by an efficient vascular network with both longitudinal and regional sources of supply.[2] The fact that some cancers have the tendency to follow nerves while others do not suggests the possibility that some obscure nutritional factor may be operative. Possibly of similar significance is the fact that cancer in a nerve sheath has a different histologic appearance than it does in other tissues; this is particularly evident in squamous cell carcinoma which invariably loses part or all of its differentiation, with the result that only rarely is keratinization observed. Basal cell and squamous cell carcinoma often are indistinguishable histologically when in the nerve sheaths even though their appearance is quite different when growing in other tissues. These peculiar features indicate that undoubtedly there is much that is not understood about the mechanism of this mode of cancerous spread.

Obviously the tendency to follow nerves would tend to have an adverse effect on the prognosis except when excision is microscopically guided as by the chemosurgical method. Even then, the prognosis in some cases may prove hopeless as it did in two instances in which the perineural extension followed the facial nerve into the stylomastoid foramen. Cases of carcinoma of the lower lip with perineural extension into the mental foramen and thence along the inferior dental canal may also present formidable though often not unsurmountable difficulties.

Cancers with Affinity for Lymphatic Vessels

Although it has long been known that some carcinomas of the breast[27] and some melanomas may spread by permeation through the lymphatic vessels, this mode of spread apparently is not so well known in connection with cancer of the skin.

Spread of carcinoma by permeation through lymphatic vessels may occur in two different ways. Either it may spread as a sheet of cancer by permeation of the small vessels of a lymphatic plexus, or it may follow one or more of the larger lymphatic vessels. The tendency to follow lymphatic plexuses is not infrequently observed in and around the nose and in the scalp (Fig. 7), while the tendency to follow the larger trunks is most commonly observed in the upper cervical and preauricular regions (Fig. 164).

Permeation by continuity through lymphatic vessels may be observed in either basal or squamous cell carcinoma. Some of the basal cell carcinomas which invade dermis do so in part by permeation through the lymphatic plexuses in the subpapillary layer. Since basal cell carcinoma does not metastasize, the presence of cancer in the lumens of lymphatic vessels is of little prognostic import as long as every extension is followed out microscopically (Figs. 29 and 164). However, the presence of squamous cell carcinoma in the lymphatic vessels is of serious significance because of the danger of metastasis.

Although the tendency of some cutaneous melanomas to spread embolically within the lymphatics at the periphery of the primary neoplasm is well known, the fact that some squamous cell carcinomas may spread in this manner is not so well known. Fortunately, the phenomenon is rare. In the present series of



Fig 164 (A) Basal cell carcinoma which had recurred after electrodesiccation and surgical excision. There were downward extensions in several large lymphatic vessels in the preauricular region. (B) Granulation tissue after chemosurgical excision. Arrow shows source of tissue for photomicrograph. (C) Photomicrograph of a lymphatic with contained clump of carcinoma cells (arrow) There was no metastasis or recurrence after six years.

1 734 cases of squamous cell carcinoma, peripheral embolic spread was observed in five instances. In one case there was a solitary nodule (Fig 54) but in the other four there were multiple nodules (Fig 165) Since the entrance of emboli into the lymphatic vessels predisposes to metastasis in the regional nodes, treatment in such cases usually should include dissection of the regional nodes as well as the removal of a wide zone around the primary lesion.



Fig 165 Squamous cell carcinoma with multiple satellite nodules due to embolic deposits in the lymphatics of the skin. Axillary metastases were resected by Dr E. R. Schmidt but the patient died of internal metastases after six months

Cancers with Affinity for Blood Vessels

The rarely observed tendency of some cancers to extend along the blood vessels may be manifested in two ways (1) by invasion along the adventitia of arteries and veins, and (2) by permeation through the lumens of the vessels.

A noteworthy degree of selective affinity for the adventitia has been observed in ten cases of squamous cell carcinoma and in two cases of basal cell carcinoma. Usually the degree of selectivity is slight, but in several cases the adventitial invasion extended 2 or 3 mm. beyond the rest of the advancing edge of the cancer (Fig 166A)

Carcinomas with a tendency to spread by permeation in the lumens of blood vessels are extremely rare. The present series includes two cases, one of squamous cell carcinoma, and one of basal cell carcinoma. In the latter case many arteries and veins in the region of the nasolabial fold were permeated and in the deeper portions of the neoplasm the downgrowths were exclusively intravascular (Fig 166B) There was no evidence of metastasis after five years. However in the patient with squamous cell carci-

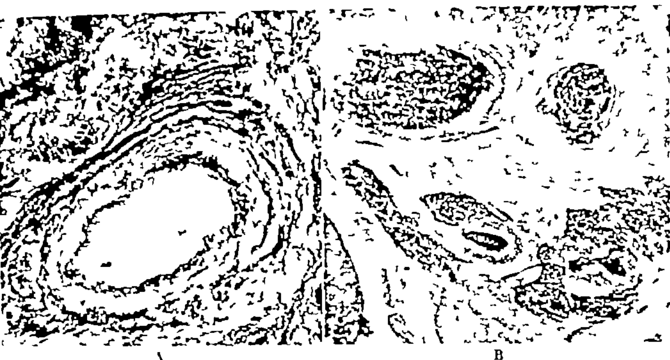


Fig 166. (A) Photomicrograph showing squamous cell carcinoma in the adventitia of a blood vessel in the nasolabial fold area. (B) Photomicrograph showing basal cell carcinoma located exclusively in the lumens of the blood vessels in the nasolabial fold area. Neither patient developed metastasis or recurrence after six years.



Fig 167 (A) Squamous cell carcinoma, recurrent after radium and x ray treatment. (B) Reconstruction of the cancer showing extensions (1) into the roof of the antrum and thence through the floor of the orbit (2) along the hard palate, and (3) into the floor of the nasal cavity An extension not shown here was in the lumen of an artery in the upper lip The patient died of cerebral metastasis after two years but there was no recurrence at the primary site

noma, fatal cerebral metastasis developed doubtless owing to emboli from the intravascular extension (Fig 167)

Cancers with Irregular Spread but with No Specific Tissue Affinities

It is common to observe the very irregular invasion of a cancer into the surrounding tissues even though little or no specific affinity for any particular tissue structure can be demonstrated (Fig 167) Apparently this is because of the considerable local variation in the mechanical and nutritional conditions which favor permeation by neoplastic tissue

As would be expected dense tissues such as bone, cartilage tendons, and aponeuroses, offer

a barrier to the spread of neoplasms. For example, a sarcoma of the scalp spread widely over the top of the cranium before it penetrated the bone and then it followed two paths of reduced resistance one, through a trephine hole (the site of a previous biopsy) and the other through the coronal suture line. If there are joints between adjacent bones, such as those of the tarsus, the neoplasm will penetrate deeper into the joints than into the bone (Fig 158) If there is a choice, cancer tends to penetrate bone where it is thin rather than where it is thick. Thus cancer in the roof of the antrum usually extends into the orbit through the thinnest bone about 3 cm. posterior to the rim of the orbit (Figs. 122 and 167)

As was mentioned in the section on spread along fascial planes, muscle also may constitute a significant barrier to the spread of cancer This apparently is not due to any particular antagonism of muscle tissue for cancer because in some cases cancer has been observed to enter a muscle bundle and spread for some distance along its length. The effect probably is predominantly mechanical. This conclusion is borne out by the frequent observation that cancer spreads more readily along the long direction of a muscle than it does in a direction perpendicular to the muscle fibers.

Not infrequently cancer is observed to extend more readily in the direction of softer tissues. This is commonly seen in lesions on the root of the nose and in the inner canthal regions where the neoplasms often extend farther in the direction of the soft tissues of the eyelids than it does in the direction of the firmer tissues of the nose (Figs. 40 41 and 42)

External factors also may influence the direction of the spread of cancer For example, in a case of basal cell carcinoma just lateral to the depression made by the nosepiece of the glasses, the neoplasm was found to have followed around the lower edge of the depression. Apparently the constant pressure of the glasses had hindered the spread of the cancer through the depressed area.

The spread of cancer through tissues which have been heavily irradiated with x rays or radium is often less rapid than through adjacent unirradiated tissue. Here there probably is a combination of the mechanical barrier imposed by the scar tissue and the nutritional deficiency occasioned by the closure of vessels owing to endarteritis.

Subcutaneous fat, with its relatively poor blood supply does not provide particularly favorable conditions for neoplastic invasion therefore, downgrowths often may be observed to follow the fibrous septa which join the skin to the deep fascia. It is difficult to determine whether this preference is due to the presence of mechanical cleavage planes in the fibrous tissues or whether it is due to the better nutritive conditions occasioned by the blood and lymph vessels which traverse these septa. Probably both mechanical and nutritive factors are operative.

Comment

From the standpoint of therapy the chief significance of the fact that many cancers send out "silent" extensions is that these outgrowths, if not recognized, may be the cause of recurrence following surgical or radiation treatment. To combat this possibility the experienced cancer surgeon removes a wide zone of apparently normal tissue at the periphery while the radiotherapist irradiates not only the clinically detectable mass but also an extra zone at the periphery With the chemosurgical method, on the contrary it is unnecessary to remove extra tissue beyond the microscopically demonstrated limits of the neoplasm. Almost always, the invading strands of cancer at the periphery are in continuity with the main mass and hence their eradication is assured by the microscopic guidance afforded by the chemosurgical technic.

Unrecognized outgrowths frequently are associated with neoplasms having a high degree of invasiveness. As would be expected the slender strands or thin sheets which characterize the advancing edge of a highly invasive cancer would be much less visible to the naked eye than the lobular outgrowing masses which characterize the less invasive neoplasm which grows more by expansion than by infiltration.

While the quantitative variation in the invasiveness of cancer is widely recognized, it is less well known that there also is a qualitative variation in invasiveness. That is, one cancer

may have a decided affinity for one tissue while another cancer of the same histologic type may prefer to spread through another kind of tissue.

By what mechanism does cancer select one pathway of spread in preference to another? Naturally there is the circumstance of position which allows the neoplasm to have access to the tissue structure in question Probably this factor partially accounts for the high incidence of cancers which show affinity for the dermis because this is the first tissue encountered by the invading carcinoma of the skin. Necessarily before a cancer can follow a fascial plane periosteum, perichondrium or other deeply situated tissue it must invade to the level of these structures. Ordinarily cancers with affinity for nerve sheaths do not follow these structures until fairly large nerves are encountered perhaps this partly explains the great frequency of perineural spread associated with carcinoma of the parotid gland which lies in close proximity to the facial and other large nerves, and with carcinoma of the prostate which has a rich nerve plexus.

However there are other deciding factors besides position, because many cancers which have had access to these various structures have exhibited no particular affinity for them. Whether or not a given cancer is destined to spread in some specific tissue seems to be an inherent characteristic of the individual neoplasm, and it is impossible to predict definitely the pattern of spread in the individual instance. The only allowable generalization is that strong specific tissue histotropism is much more likely to be observed in association with the more highly invasive carcinomas whether of basal squamous or other cell type than it is in less invasive neoplasms.

It seems probable that both mechanical and nutritional factors are operative in determining the direction of neoplastic spread. That there are numerous tissue planes in which injected fluids tend to spread out more readily than in adjacent tissues is easily demonstrable, and it is not surprising that the same planes should offer diminished resistance to the spread of some cancers. However it is often along these planes that the blood and lymph vessels travel and it may be argued that these supply more favorable nutritive conditions for neoplastic growth Moreover some firm tissues such as the dermis would not readily allow passage of injected fluids but they often provide a favored pathway of carcinomatous spread Probably a combination of mechanical and nutritional factors always is operative but one or the other may predominate as determined by the location and by the characteristics of the individual neoplasm

It may be speculated that the various factors which are responsible for the invasiveness of cancer may vary in such a way that one cancer may tend to prefer one tissue while another prefers a different tissue The factors which may condition the invasiveness of cancer are (1) progressive multiplication of cells (2) motility of cells (3) diminished adhesiveness of cells and (4) tumor metabolites.[144] Since progressive multiplication of cells is a characteristic of all cancers it is unlikely that variations in this quality would have any great effect on the selection of the tissue into which the cancer invades. However the other three factors conceivably could.

That the cells of some cancers exhibit motility of an ameboid type can be demonstrated with fresh preparations and with tissue cultures. It is likely that the greater the motility of the cells the greater the invasiveness of the neoplasm but the question as to whether variations in motility might have an effect on the type of tissue a given cancer would preferentially invade remains to be determined. Similarly there is evidence that the less the adhesiveness of the cells, the greater the invasiveness of the cancer but just how diminished adhesiveness would affect the pattern of neoplastic spread also remains to be elucidated by further investigations. It would seem that cancers which form satellite nodules due to spread by embolism through the skin lymphatics would be composed of cells with increased motility and diminished adhesiveness. However this is surmise as is any attempt to correlate the pattern of spread with these factors without more information than is now available.

There has been a number of investigations on the effect of diffusable metabolites on invasiveness. Following Duran Reynals [24] demon

stration of a spreading substance in cancer tissue the possibility was suggested that neoplastic invasion might be affected by this substance which later was proved to be hyaluronidase. However Coman's group[13,14] was unable to find any correlation between the degree of invasiveness and the content of hyaluronidase. *In fact, some workers feel that the hyaluronidase* content of tumors is largely of bacterial origin.[39] *However even if hyaluronidase were proven to* augment tumor invasiveness, the explanation of the variation in specific tissue affinities still would require further elucidation. Conceivably quantitative variations in the hyaluronidase content could determine what tissue the cancer would tend to invade and it even is conceivable that hyaluronidase might have qualitative variants which could accomplish the same thing.

It has been demonstrated that the adhesion of cells to one another is dependent upon slightly soluble calcium compounds which can be removed in vitro by means of calcium fixing compounds such as sodium citrate. It is conceivable therefore that cancers might produce a diffusible metabolite which could increase invasiveness by virtue of an ability to fix calcium. If this could be proved it might be possible to go further and correlate quantitative levels of this substance with the selection of host tissues.

Although it is difficult to conceive of plausible mechanisms to explain why one cancer prefers to invade one type of tissue rather than another the fact remains that such tissue preferences on the part of some neoplasms do exist. Other cancers have no definite tissue affinities and yet they also may invade in an irregular and unpredictable manner. Regardless of how these "silent" extensions develop it is important that their frequent occurrence be appreciated by everyone who treats patients with cancer. The ever present possibility that these extensions may occur is the chief reason for the development of the chemosurgical technic with its microscopic control of excision.

PART II

BENIGN TUMORS AND PRECANCEROUS LESIONS



CHAPTER 22

Benign Tumors of Epithelial Origin

A NUMBER of benign epithelial growths of either neoplastic or nevoid nature are commonly seen in a chemosurgery clinic Being benign and usually well demarcated from the surrounding tissues, these lesions often are most expeditiously treated by simple excision and suture or by excision and cauterization with dichloracetic acid. However the microscopic control afforded by the chemosurgical method occasionally is useful. This group of tumors is derived either from the surface epidermis or from the skin appendages which include the sebaceous glands, the sweat glands, and the hair follicles.

Nevus Verrucosus

This papillomatous lesion usually is present at birth but over the years it gradually enlarges and becomes more deeply pigmented Since malignant change is rare, removal usually is for the sake of appearance Histologically the tumor is composed largely of epithelium which is thrown up in papillomatous folds. Usually most of the melanin pigment is in the basal layer of the epidermis. Occasionally there may be associated pigmented nevocellular elements.

Although the lesion may be considerably elevated it usually is superficial. Therefore conservative excision under local procaine anesthesia followed by light cauterization with dichloracetic acid is adequate. The exact extent of the abnormal epithelium is readily visualized because the white color of the cauterized epithelium contrasts with the grayish color of the cauterized fibrous tissues. Removal may be carried out so conservatively that if hairs are present in the lesion it may be feasible to preserve the bottoms of the hair follicles and thus avoid a bald spot (Fig 168)

Nevus Sebaceus

Usually present at birth or at an early age this nevoid abnormality of the sebaceous glands tends to occur singly on the scalp face or elsewhere as a slightly elevated yellowish placque with a smooth though furrowed surface Histologically the lobules of glandular tissue are hyperplastic and the decay to fatty detritus in the center of the lobules is less in amount than in normal sebaceous glands

The abnormal tissue is sufficiently readily visualized to give assurance of complete removal by excision and cauterization with dichloracetic acid. If there is any doubt as to the diagnosis, frozen sections should be made. Rarely is there associated basal or squamous cell carcinoma but when there is chemosurgical excision is indicated

Senile Sebaceous Nevus

These lesions commonly occur on the face after the age of forty as small nodules or placques with flat or umbilicated surfaces. Upon blanching with pressure the tissue is cream colored as contrasted with the pearly color of basal cell carcinoma. Histologically the lesions are composed of sebaceous glands which are indistinguishable from normal glands except for the hyperplasia.

Removal is by excision followed by cauterization with dichloracetic acid. There is no need for microscopic confirmation of the completeness of removal because the hyperplastic glands are readily visualized on the cauterized sur



Fig 168. (A) Nevus verrucosus. Several similar lesions had been present on the top of the head since birth but since they were unnoticeable under the hair the patient did not want them removed. (B) Healed lesion. The bottoms of the hair follicles were purposely preserved in order to avoid a bald spot.

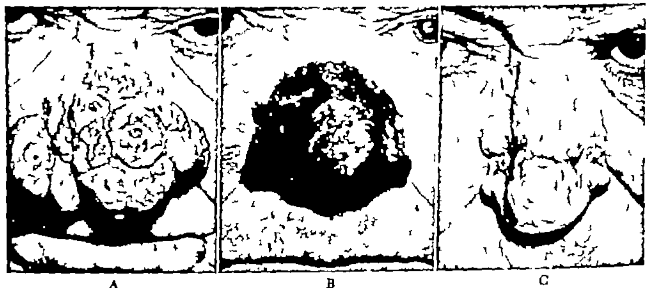


Fig 169 (A) Rhinophyma. After the hyperplastic and cystic masses were pared off hemostasis was secured with dichloracetic acid and squares of zinc chloride-impregnated gauze squares. (B) Granulation tissue after separation of the cauterized tissue. (C) Healed lesion after two months.

face. Frozen sections may be made if there is doubt as to the diagnosis.

Rhinophyma

This condition is a form of rosacea with extreme hyperplasia and hypertrophy of the sebaceous glands and the surrounding fibrous and vascular tissues. The bulbous masses of tissue may be pared off and hemostasis secured with dichloracetic acid and zinc chloride fixative impregnated gauze squares (Fig 169) In some cases excision followed by plastic repair may be preferable.

Other Tumors of the Sebaceous Glands

Other sebaceous gland tumors such as sebaceous adenoma, and nevus epitheliomatosis sebaceous capitis are rare lesions which have

not yet come to the attention of the author However the technics outlined in the preceding paragraphs should be applicable

Syringoma or Syringocystadenoma

These tumors of the sweat glands often are multiple but may be single In the latter event the nodule may resemble basal cell carcinoma clinically (Fig 170A) However, the histologic picture is diagnostic. In the dermis there are numerous small cysts lined with a double layer of small epithelial cells derived from the ducts of sweat glands of either eccrine or apocrine type. The cysts may be round or oval or they may be elongated forming structures shaped like a comma Numerous slender strands of small cells also may be present.

The well demarcated lesions often can be conservatively excised and cauterized with dichloracetic acid. However in some cases the slender strands of epithelial cells may spread further into the surrounding dermis than would be expected from the clinical appearance When this possibility is suggested by the microscopic appearance of the frozen sections chemosurgical excision may be advisable to assure complete removal (Fig 170) Occasionally there is associated basal cell carcinoma in this event chemosurgical excision is indicated

Syringocystadenoma Papilliferum

This is a sweat gland nevus which occurs singly or in groups in areas of intense perspiration Microscopically the sweat glands are cystic in places and there are villi like papillomatous projections into the lumens There usually is a mild inflammatory reaction with infiltration of plasma cells. The nodules may be excised and cauterized with dichloracetic acid

Vulvar Hidradenoma

This tumor apparently originates from the apocrine glands of the labia majora or labia minora Microscopically it is composed of reticulated cords of epithelial cells The lesion may be removed by excision followed either by suture or by cauterization with dichloracetic acid Chemosurgical treatment is needed only when there is doubt as to the completeness of removal

Mixed Tumors of the Sweat Glands

These tumors closely resemble the mixed tumors of the salivary glands and although they are benign troublesome recurrences may develop if removal is incomplete. For example, one of the author s patients had a mixed tumor which had recurred on the cheek after surgical excision elsewhere and had extended into the

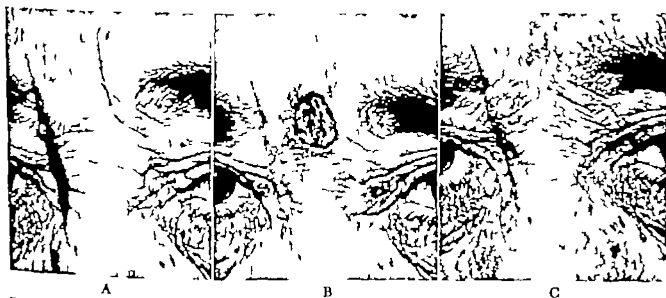


Fig. 170 (A) Syringoma which resembled basal cell carcinoma clinically (B) Granulation tissue after chemosurgical excision. The syringoma extended 3 mm. further into the dermis at the inferior edge than was expected from the clinical appearance. (C) Healed lesion. There was no recurrence after six years.

floor of the nasal cavity Chemosurgery with its microscopic control proved very valuable in determining the exact extent of the neoplasm which had spread farther than indicated by the clinical appearance. There was no evidence of recurrence after three years.

Cylindroma

This benign tumor usually is multiple and may involve large areas of the scalp giving rise to the term "turban tumors." However cylindroma may occur singly as it did in one of the author's patients. In this case the tumor was on the forehead at the hair line. It was chemosurgically excised and there was no recurrence or further tumor development after three years. Since turban tumors usually develop in young adult life and grow slowly to considerable size their removal at an early stage is advisable. Whether this is done by excision and suture, by excision and cauterization with dichloracetic acid or by chemosurgical excision depends upon such factors as size, location, and sharpness of demarcation. Microscopically these benign tumors *resemble basal cell carcinoma but there is* a characteristic hyalinized connective tissue membrane around each clump of cells.

Trichoepithelioma

As the name implies, these tumors are of hair follicle origin. Other terms for the disease are multiple benign cystic epithelioma and epithelioma adenoides cysticum. As these descriptive terms indicate these neoplasms are benign, multiple, adenoid, and cystic in nature They usually appear at puberty and grow slowly to form disfiguring nodules on the face, scalp and neck (Fig 171) The extent of the well



Fig 171 (A) Trichoepitheliomas in such large numbers that removal had to be carried out in several sittings. (B) Appearance of lesions immediately after removal of twenty-eight lesions by excision and cauterization with dichloracetic acid. A total of 115 lesions had been removed in five sittings. Several more sessions were required to eliminate all of the tumors.

demarcated tumors is readily determined by gross examination after excision and cauterization with dichloracetic acid. A magnifying loupe aids visualization and assures complete removal. The tumors may be so numerous that the removal of two or three dozen lesions at each of several sittings may be necessary. If malignancy is suspected, frozen sections are made; if basal cell carcinoma is found, as it is on rare occasions, chemosurgical treatment is instituted.

Calcifying Epithelioma

These bony hard, sharply circumscribed tumors in the deep dermis and subcutaneous fat apparently develop from embryonic rests of epithelial cells which have a tendency to differentiate to keratotic hair cells. Following the retrogressive metamorphosis of the epithelial elements, calcification or even ossification takes place. Some of these tumors have been chemosurgically removed to rule out malignant disease. However, since they are inherently benign, surgical excision often is the treatment of choice.

Pseudoepitheliomatous Hyperplasia

Though not a true neoplasm, this type of hyperplasia may closely simulate squamous cell carcinoma both clinically and microscopically. The condition may occur in chronic granulomas such as bromoderma, iododerma, lupus vulgaris and blastomycosis. It may develop at the edges of chronic ulcers such as occur in old burn scars or stasis ulcers. The so-called "self healing squamous cell carcinomas" or kerato-acanthomas are thought by Allen[3] and others to be merely pseudoepitheliomatous hyperplasia occurring in epidermal inclusion cysts or coalescent comedones.

The microscopic findings include irregular invasion of the dermis by epidermal cell masses with pearl formation and numerous mitoses. However, the squamous cells remain well differentiated and they do not exhibit individual cell keratinization or nuclear hyperchromasia such as occurs in squamous cell carcinoma. Moreover, there is invasion and destruction of the hyperplastic epithelial downgrowths by leukocytes to a greater extent than ordinarily is seen in carcinoma.

Numerous lesions in which pseudoepitheliomatous hyperplasia was present have been removed chemosurgically. In some cases the lesions were removed in order to rule out carcinoma; in others the purpose was to remove a precancerous lesion while in others the object was to eliminate a chronic infection which had initiated and perpetuated the hyperplasia. Since the condition is benign, simple excision followed by cauterization with dichloracetic acid may suffice, but when there is doubt as to the exact extent of the hyperplasia or the initiating infectious process or when malignancy is suspected, the microscopic control of the chemosurgical method is useful.

CHAPTER 23

Benign Tumors of Connective Tissue Origin

ALTHOUGH most benign tumors of connective tissue origin can be removed satisfactorily and reliably by ordinary surgical means, there are occasional lesions for which chemosurgical technics are advantageous For example the neoplasm may be so located that excision with a satisfactory margin is difficult to accomplish, or the periphery of the neoplasm may be difficult to outline grossly despite the benign nature of the tumor or there may be doubt as to whether the tumor is benign or malignant.

Fibroma

Fibroma of a truly neoplastic nature is uncommon in the skin but is more common in the underlying fibrous tissues. Removal is advisable since the tumor may grow progressively and lead to masses of troublesome size. Furthermore, fibroma occasionally leads to sarcoma (Fig 155) Lesions which are well circumscribed usually are best removed by excision and suture However poorly defined lesions in some locations may be more certainly and more conservatively removed by means of the chemosurgical method.

Dermatofibroma and Histiocytoma

Since the histiocytes of the histiocytoma apparently mature to form the fibroblasts of the dermatofibroma, the two tumors are considered together That there is some disagreement as to the nature of these tumors is indicated by the variety of terms such as sclerosing hemangioma (Gross and Wolbach) nodular subepidermal fibrosis (Michelson) and fibroma simplex (Unna) Whatever their histogenesis, these growths rarely show progressive growth. They grow to a certain size and then remain stationary or get smaller They are most common on the extremities but may develop on the trunk or elsewhere. Usually they are small firm, grayish-brown, slightly elevated nodules but they may be depressed below the skin surface There may or may not be a history of trauma. Microscopically the dermatofibroma is composed of fibroblasts with spindle shaped nuclei and scant cytoplasm while histiocytomas are made up of fibroblasts and histiocytes. The latter have ample pale cytoplasm and ovoid nuclei. The pigment distributed through the tumor is hemosiderin. There is no encapsulation. These lesions need not be removed unless they are cosmetically undesirable or unless they exhibit progressive growth. Often surgical excision and suture can be carried out readily The lesions have been chemosurgically excised in several dozen cases with no instance of recurrence. In the occasional case in which the clinical appearance suggests possible melanoma, chemosurgical excision is preferable to wide surgical excision because if the lesion proves to be benign, removal may be conservative while if it proves to be melanoma chemosurgical excision may be continued until an appropriately radical level is reached.

A considerable number of tumors of connective tissue origin have been removed in the Chemosurgery Clinic. Some were removed surgically while sixty-two were removed chemosurgically In the latter group there were four progressively growing fibromas, thirty-one histiocytomas and twenty three dermatofibromas. In addition, four neurofibromas were removed

from patients suffering from neurofibromatosis (Von Recklinghausen's disease) There were no known recurrences of any of the tumors but since these conditions are benign no effort was made to observe the patients for an extended period

Cutaneous Tags

Small, soft nodules which frequently become pedunculated often are observed in the axillae on the neck, on the eyelids and elsewhere on the skin of individuals over the age of thirty These are merely outpouchings of the skin. Usually the epidermis is normal but occasionally the apex may become hyperkeratotic The lesion may become inflamed as a result of abrasion and infection. Usually the pedunculated lesions are readily snipped off with scissors without local anesthesia. Only if the lesions are large are sutures or cauterization of the base necessary If the lesions are sessile cauterization with dichloracetic acid is adequate unless the lesion is too thick in which case excision and suture or excision and cauterization with dichloracetic acid may be preferable Microscopically controlled chemosurgical excision is unnecessary

Keloids

The fact that postchemosurgical wounds usually epithelize rapidly with resultant soft, smooth scars suggested that the chemosurgical method might be useful for the removal of keloids. As it has turned out, the results are good in the treatment of the hypertrophic scars which result from unusual irritation of the wound during healing but in the treatment of true keloids, such as may result from trivial injuries in some individuals, the end result usually is no better than the original keloid.

Any wound which develops exuberant granulation tissue during the course of healing is likely to develop hypertrophic scars. Exuberant granulation tissue may be produced by any source of irritation such as infection or the presence of a foreign body A number of examples may be cited. In several cases, the patients had excessive scars from the irritation produced by low grade infection during the healing of furuncles. In another there was an excessive scar from a granuloma pyogenicum which finally healed after a long delay In still another the excessive scar apparently was the result of irritation of hairs growing from the adjacent skin and protruding into the granulation tissue One patient had an excessive scar around a small fragment of steel In another excessive scar seemed to be a result of the irritation produced by deposits of calcium in old thermal burns In all these cases the chemosurgical removal of the excessive scar led to improved scars.

On the other hand a patient with true keloids following furunculosis developed the same amount of keloid within a few months after chemosurgical excision Similarly a patient with a true post traumatic keloid on the helix of the ear suffered a recurrence after chemosurgical excision In such cases, chemosurgical excision should be followed by irradiation with radium or filtered roentgen rays to retard the proliferation of the fibrous tissue Irradiation should be delayed for two or three weeks after complete epithelization and should be administered in small repeated doses. In case there is a question as to whether or not the patient has a tendency to form true keloids, the irradiation may be delayed until there is beginning elevation of the scar Ordinarily chemosurgical removal of keloids is not indicated for lesions that can be surgically excised and closed with sutures, but the method is useful for lesions which cannot readily be closed primarily as exemplified by the keloid of the helix of the ear just mentioned

Microscopic guidance of the excision of hypertrophic scars and keloids is unnecessary as the amount of tissue to be removed may be judged by the gross appearance and consistency of the tissue

Osteoma

Since the chemosurgical technic can be used to microscopically determine the nature of osseous tissues the method is useful for the removal of osteomas in certain accessible locations (Fig 172) The layers of fixed bone can be removed with a chisel or rongeur and microscopic sections made to determine the level at which normal bone is encountered The final

layer of fixed bone usually separates from the underlying unfixed bone in approximately three weeks leaving a well vascularized surface over which the skin rapidly grows. Exostoses may be treated in the same manner

As yet no primary neoplasms of bones other than the cranium have been removed chemosurgically There is reason to believe however that the method might be useful in certain selected cases in which the benign or malignant neoplasm is limited to accessible bony surfaces when there is a question of neoplasia associated with the bone formation.

Chondroma

Chondromas and osteochondromas may blend into the adjacent normal cartilage in such an imperceptible manner that the microscopic guidance of the chemosurgical technic may be useful to determine the exact extent of the neoplasm An example of this was an osteochondroma which involved the ear cartilages



A B

Fig. 172 (A) Osteoma of two year's duration with beginning obstruction of the ear canal (B) Healed lesion two years after chemosurgical excision. The layers of fixed bone which were removed with a small chisel were sectioned to indicate when normal bone was reached.

such as on the tibia, humerus or the bones of the hands and feet. In some cases the conservative approach which is made feasible by the chemosurgical technic might eliminate the necessity of more radical procedures.

Calcific and osseous deposits in the skin and subcutaneous tissues may arise either on the basis of embryonal rests (osteoma cutis) or on the basis of abnormal conditions such as thermal or roentgen scars. Another source of calcium deposition is the so-called calcified epithelioma of Malherbe In certain cases the chemosurgical technic may be useful for the removal of the abnormal deposits because although the extent of the calcified tissue is readily determined grossly the microscopic sections are useful following removal in this manner there was no evidence of recurrence after two years.

The chemosurgical technics also are useful for the removal of areas of perichondritis which may produce painful nodular growths on the ear (chondrodermatitis nodularis chronica helicis) In such cases prompt healing takes place after removal of the nodule along with a small pellicle of cartilage.

Xanthoma

Most xanthomas are not true neoplasms but consist of nodular or placque like collections of cholesterol in histiocytes within the skin and subcutaneous tissues. The structures most commonly involved are the eyelids (xanthoma

palpebrarum or xanthelasma) In this location the method of removal depends on several factors. If the eyelids are not deeply pigmented the simplest means of destruction is the simple application of dichloracetic acid or a saturated solution of trichloracetic acid Accurate application of the acid is accomplished with a sharp-pointed cotton tipped applicator If the placque is too thick to be adequately penetrated some of the cauterized tissue may be excised and another application made Larger lesions may be excised under local anesthesia and the area cauterized with dichloracetic acid or closed with sutures. Following cauterization no dressings are necessary The cauterized tissue separates spontaneously in a week or so after which mercurochrome is applied until healing is complete. The scars are barely visible unless the eyelids are heavily pigmented in which case areas of lighter color remain for a long time Therefore in patients with dark eyelids excision and suture usually is preferable.

Xanthomas in other sites and of other types are much less common while progressively growing xanthomas are rare The removal of these lesions by chemosurgical methods is feasible, but the choice of treatment depends upon factors such as the location, size, clinical course and histologic type In some cases the conservatism made possible by the chemosurgical technic is advantageous for example in a patient with a xanthoma on the tip of the index finger a good functional and cosmetic result was obtained Similarly in a patient with a xanthoma on the tip of the nose the resulting scar and defect were unnoticeable Xanthomas exhibiting infiltrative growth may require microscopically controlled chemosurgical excision for assurance of complete removal

Other Tumors of Mesodermal Origin

A few lipomas, myxomas, leiomyomas and rhabdomyomas have been observed in the Chemosurgery Clinic. Usually these benign tumors are so well circumscribed that surgical excision and suture is preferable but in some instances they were removed chemosurgically with satisfactory results.

Giant cell tumors of tendon sheaths are really not true neoplasms but are a histiocytic and giant cell reaction to synovitis one of these tumors was chemosurgically excised from a finger with a good result.

The so-called synovial cysts such as commonly occur on the fingers are not lined with either synovial or epithelial cells. Rather they consist of a myxoid degeneration of the subcutaneous tissues. Good results usually are obtained by unroofing the cyst, removing the mucoid contents and cauterizing the inside of the cystic space with dichloracetic acid. By probing the space with a small applicator the exact extent of the degenerative process may be determined often the cystic space extends farther peripherally than expected. Care should be exercised not to apply too much of the acid because this might lead to damage of the underlying joint structures. If the lesion recurs the treatment may be repeated.

CHAPTER 24

Hemangioma

THE chemosurgical technics are useful in the treatment of hemangiomas of several types. Microscopic control of excision is unnecessary because the hemangiomatous tissue is readily visualized grossly since the blood in the vessels becomes black when acted upon by the fixative chemicals while the surrounding fibrous tissues become a contrasting white.

Nevus Vasculosus (Strawberry Mark)

This is the hemangioma most commonly treated chemosurgically. The technic varies according to circumstances. In some cases it may be expedient to apply dichloracetic acid and zinc chloride prior to the excision of the first layer of the hemangiomatous tissue. This chemosurgical technic allows excellent visualization of the hemangiomatous tissue and may be advisable where the greatest possible degree of conservatism is desired, as for example, in a patient with a hemangioma of the helix of the ear (Fig 173).

More rapid removal may be accomplished, however by the excision of the neoplasm under local anesthesia followed by cauterization with dichloracetic acid. The chemically treated tissues usually exhibit a satisfactory contrast between any residual hemangioma and the surrounding fibrous tissues. If a focus of hemangioma is observed to persist, another layer is excised from that area and the tissues again are cauterized. This process is repeated until all of the hemangioma has been removed (Fig 174). The entire procedure is completed in one sitting hence there is no need to keep the zinc chloride fixative in place for prolonged periods. This is an advantage in infants who might scratch off the dressing and carry the

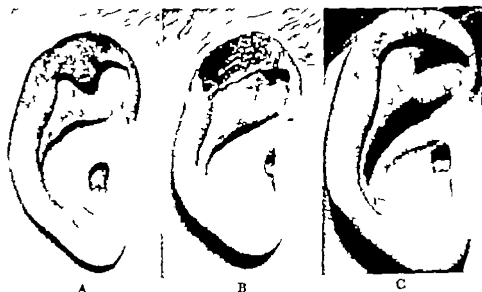


Fig 173 (A) Hemangioma in a boy five years old. It had continued to grow despite treatment with radium. (B) Granulation tissue after chemosurgical excision. Only a slender strip of cartilage had to be removed. (C) Healed lesion three years later

fixative away from the site of application with consequent reduction in penetration and possible damage to sensitive neighboring structures such as the eye.

In cases in which there has been considerable bleeding during excision the blood may make it difficult to see if removal has been complete. In this circumstance the application of the zinc chloride fixative for an hour or so makes it possible to remove a thin layer of fixed tissue in order to definitely determine whether or not any of the hemangioma remains.

Following removal of hemangiomas from the face and other regions the scars ordinarily have a satisfactory appearance. The scars on the scalp are devoid of hair but the contraction of the scar reduces the size of the bald spot (Fig 175)

Although most hemangiomas are seen in infants and children, those which involve the



Fig. 174 (A) Hemangioma in an Infant four months old. The lesion was excised under local anesthesia and the area cauterized with dichloracetic acid. (B) Healed lesion after one year



Fig 175 (A) Hemangioma, cavernous type, In an infant four months old. (B) Granulation tissue after chemosurgical excision. (C) Healed lesion eight months later

vermilion borders of the lips are fairly commonly encountered in adults. These need not be removed unless they become cosmetically objectionable show rapid growth or become ulcerated. Usually the soft, compressible tumors of dark red or bluish red color are readily



Fig 176. (A) Hemangioma which formed a soft, blue mass on the lip of a woman seventy years old. (B) Granulation tissue after chemosurgical excision. (C) Healed lesion. There was no recurrence after nine years.

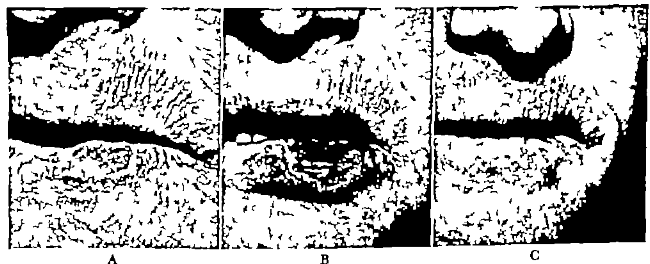


Fig 177 (A) Ulcerated and infected hemangioma which resembled carcinoma clinically It had not improved appreciably after radium treatment. (B) Granulation tissue after chemosurgical excision. (C) Healed lesion. There was no recurrence after five years.

recognized clinically (Fig 176) However when they become ulcerated and infected they may be mistaken for carcinoma (Fig 177) In either event the cosmetic results following chemosurgical excision are excellent.

Hemangiomas or "juvenile angiofibromas of the nasopharynx can cause distressing obstruction in children hence their removal may be imperative. In one case however the tumor continued to enlarge after repeated attempts at removal with the endotherm knife, and destruction with radium needles and radon seeds in another clinic. Accordingly chemosurgical removal of the large mass was carried out. Owing to the relative inaccessibility of the tumor the layers of fixed tissue could not be excised in the usual manner therefore the fixative was applied and each layer of fixed tissue was allowed to separate spontaneously By this means the large mass was eradicated

after six months of intermittent treatment and there was no recurrence after seven years.

Hemangiomas in the vagina or in the vicinity of the urethra (urethral caruncles) may be excised under local anesthesia the area cauterized with dichloracetic acid and if necessary, with zinc chloride fixative. Lesions around the urethra may require the use of an indwelling catheter while chemosurgical treatment is under way

One hundred patients with hemangiomas have been treated with the technics described above The number of lesions in the various sites were as follows face, scalp and neck, thirty three nose eight ear two eyelids, five extremities and trunk, twenty five mouth three labium majus one and lips, twenty three. The hemangiomas were eradicated in *all of* the patients except in four who had lesions of such large size that removal of only part of the tumor was indicated. Most of the vascular tumors were classified histologically as capillary or capillary-cavernous hemangiomas but several were classified as cavernous hemangiomas. In some cases the proliferation of endothelial cells overshadowed the dilated capillaries.

Chemosurgical technics are not intended to be used to the exclusion of other methods for the treatment of hemangioma. For example some lesions may be so located that surgical excision with closure is preferable while others may be more suitable for injection with sodium morrhuate or other sclerosing agents. In still others radium or roentgen therapy or freezing with solid carbon dioxide may be indicated Hemangiomas vary so widely that it is desirable to have available a variety of modalities from which to choose the most suitable treatment for the individual case Occasionally combinations of the different types of treatment may be useful Hemangiomas of infants not infrequently disappear spontaneously by the age of six or seven years. This is especially likely to occur if the tumor has exhibited active growth during the first few months It is justifiable therefore, to reassure the anxious parents and to await spontaneous regression in cases in which the removal of the lesion is likely to leave a scar which is cosmetically or functionally objectionable.

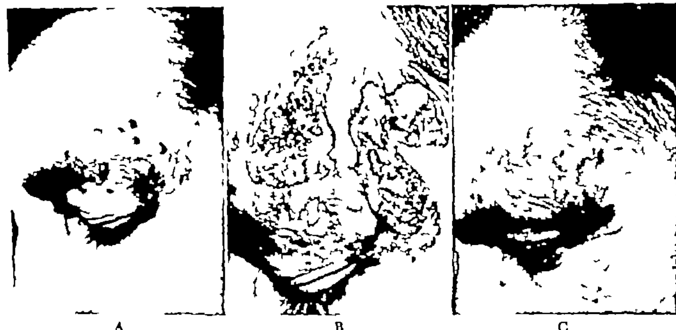


Fig 178 (A) Nevus flammeus with angiomatous nodules in a man twenty two years of age (B) Granulation tissue after chemosurgical excision. (C) Healed lesion after two months.

Nevus Flammeus (Port Wine Mark)

Patients with this hemangioma in association with angiomatous nodules have been treated chemosurgically with satisfactory results (Fig 178) However, the method is useful only in

lesions of moderate size because the scar formation following the removal of large lesions would be objectionable.

Nevus Araneus (Spider Nevus)

This vascular nevus may be treated either by the application of dichloracetic acid and zinc chloride to the central artery or by the excision of the tip of the vessel under local anesthesia following by the application of dichloracetic acid on a pointed cotton tip applicator The capillaries which radiate from the central feeder vessel need not be removed because they collapse as soon as the central arteriole with its abnormal pressure is eliminated That there is arterial pressure in the central vessel is indicated by the spurting which often occurs when the tip of the vessel is excised. Since treatment may be very conservative the resultant scars usually are practically invisible.

Senile Angiomas

These small bright red macules or papules which often occur on the trunk, face and other areas of the skin of elderly people may require removal if they are subject to trauma or if they become cosmetically objectionable Since they are completely benign, very conservative removal is adequate. This may be accomplished either by excision under local anesthesia with cauterization of the base with dichloracetic or if the lesion is small, by cauterization dichloracetic acid without prior excision.

Glomus Tumors

These are painful nodules composed of h plastic tissue of the neuromyoarterial glo which are neurovascular structures at the tion of the skin and subcutaneous ti Usually excision and suture is the me of choice. In one instance however a gl tumor was chemosurgically excised from lower leg with a satisfactory result.

Lymphangioma Circumscriptum anc Associated Hemangioma

Lymphangioma and hemangioma occasio occur in association with each other In patient this condition affected both sides o base of the tongue. A satisfactory result obtained by excision of the angiomatous t followed by cauterization of the base dichloracetic acid *By the same techn* placque of lymphangioma circumscriptum its characteristic "frog spawn" appearance removed from the dorsum of the tongue young boy The extent of the lymphangioma tissue is readily observed grossly after caute tion of the base with dichloracetic acid he complete removal is assured without the s fice of adjacent normal tissues.

CHAPTER 25

Pigmented Nevi

PIGMENTED nevi are of four main types intradermal, compound junction and blue This classification is of importance from a therapeutic standpoint because intradermal nevi practically never undergo melanomatous change while junction nevi commonly do Compound and blue nevi on rare occasions also may become melanomatous especially if subjected to trauma or irritation. In the present series of 492 lesions the incidence of the various types of nevi was as follows intradermal nevi, 84 7 per cent junction nevi, 5 8 per cent compound nevi, 5.8 per cent and blue nevi, 1 6 per cent.

Intradermal Nevi

The most frequently encountered nevus is the common mole which is termed the intradermal nevus because the nevus cells are situated in the dermis (Fig 179) Characteristically the lesion is a more or less elevated nodule or placque which usually is brown but which may be black, pink or flesh colored. The surface may be papillated and occasionally is hyperkeratotic. Small hairs or larger vibrissae often are present.

Intradermal nevi often are removed for the sake of appearance or because of inflammatory changes produced by the rubbing of an article of clothing such as a belt, shoulder strap or brassiere. Not infrequently they are removed because they are subject to repeated trauma such as may occur while shaving or while combing the hair

Nevi which definitely have the clinical appearance of the intradermal type and which have not undergone changes such as inflammation ulceration, sudden enlargement or change in pigmentation may be removed by any modality that gives reasonable assurance of complete eradication In the Chemosurgery Clinic such lesions ordinarily are simply excised under local anesthesia and the wound cauterized with dichloracetic acid When coarse vibrissae are present they should be removed by electrolysis prior to removal of the nevus If the nevus is located in an area where excision and closure with sutures may readily be accomplished this may be the method of choice also this often is the preferred method when the lesions involve the skin of the upper lip or the anterior chest where there is a greater tendency toward excessive scar formation. There probably is no danger in partial removal of intradermal nevi but nevertheless an effort should be made to remove all of the nevus. Gross visualization is facilitated by cauterization of the surface with dichloracetic acid. Microscopic control of excision is not necessary although a frozen section ordinarily is made to eliminate all doubt as to the diagnosis.

Nevi which have been irritated or traumatized or which have undergone some recent change always should be examined microscopically preferably by frozen section so further chemosurgical treatment can be carried out immediately if any involvement of the dermal epidermal junction is found. Microscopic study also is indicated in cases in which there is some doubt as to whether or not the lesion is purely of the intradermal type.

If junction nevus is demonstrated in the vertical microscopic section it is advisable to assure complete removal by the use of the microscopically controlled excision afforded by the chemosurgical technic.

After excision and cauterization or excision and chemosurgical treatment of nevi the lesion is left open. If the wound is large or in a



Fig 179 Photomicrograph of intradermal nevus.



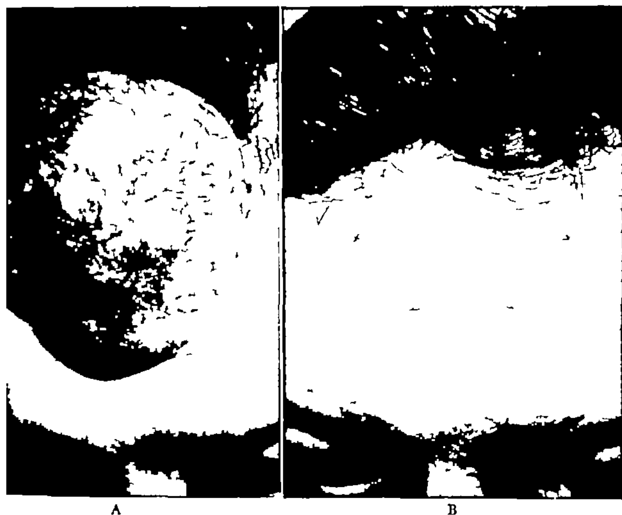
Fig. 180. (A) Intradermal nevus. (B) Granulation tissue after chemosurgical excision. (C) Healed lesion.

nt area it may be covered with a dry

In one to two weeks the cauterized ...arates and healing if not already com...kes place shortly Mercurochrome is ... to the wound to provide a protective ...ntil epithelization is complete The ...ually remain depressed below the skin ...*for a few weeks after which they grad*...tten out and assume the appearance of

was all that was necessary The cosmetic results in general were satisfactory (Fig 180) In some locations such as the forehead, the cosmetic results following chemosurgical removal of large nevi compared favorably with the results which might be expected from excision and plastic repair (Fig 181)

In several cases basal cell carcinomas were observed to have developed in association with



A B

Fig 181 (A) Intradermal nevus. (B) Healed lesion.

...rmal skin. Rarely does excessive scar ... but in patients with a keloid tendency ...on may become slightly elevated In such ...xcision and subsequent radiation with ... or roentgen rays occasionally may be ...ed.

...hese methods over 400 intradermal nevi ...emoved. In no case did melanomatous ... supervene In a few cases flecks of pig...appeared in the scar but these were so ...hat cauterization with dichloracetic acid

intradermal nevi. In one case there was an associated squamous cell carcinoma The treatment of such lesions is the chemosurgical excision of both neoplasms.

Junction Nevi

Less common than intradermal nevi, junction nevi are much more important from a preventive standpoint because of the relatively high incidence of malignant melanoma in these lesions. Characteristically junction nevi are flat



Fig. 182 (A) Junction nevus which had increased in size sixfold in 10 years. Blisters often had been produced by the shoes rubbing on the surface (B) Granulation tissue after chemosurgical excision. (C) Healed lesion five years later (D) Photomicrograph showing considerable proliferative activity in the nevus cells at the dermo-epidermal junction.

or slightly elevated smooth hairless placques which usually are either brown or brownish black but which may be slate blue or bluish black (Fig 182) Often there is a history of recent enlargement ulceration or increase in pigmentation

Because junction nevi may undergo melanomatous change chemosurgical excision is indicated not only to assure complete removal as determined microscopically but also to safely detect any possible areas of incipient melanoma If melanomatous changes are observed wider removal is indicated as described in the chapter on melanoma.

Chemosurgical excision of 34 junction nevi was carried out with no instance of recurrence or development of melanoma at the primary site. In one case however a growing lesion was chemosurgically excised from the foot and, although there was no recurrence in the primary site the patient developed metastatic melanoma in the groin. Apparently melanoma already had arisen in the junction nevus but it was missed in the microscopic sections. This case emphasizes the importance of the study of numerous microscopic sections through various parts of junction nevi in order that wide removal of the primary lesion and possibly dissection of the regional nodes may be carried out if melanoma is demonstrated

Compound Nevi

According to Allen[4] 12 per cent of nevi which have the clinical appearance of common moles show microscopic evidence of some degree of junctional involvement. In children the figure may be as high as 90 per cent.[19] Such moles are termed "compound" nevi because both intradermal and junctional components are present. It is probable that most supposed instances of melanomatous change in common moles actually were melanomas which arose in compound nevi. Hence, when a mole is subject to chronic irritation or trauma the safest course is to assume that the nevus is of the compound type and to take measures to assure complete removal This may be done by excising the nevus, cauterizing the area with dichloracetic acid and making a frozen section of the excised specimen. If microscopic examination reveals compound nevus, chemosurgical excision is carried out to make sure that all of the nevus has been removed

Blue Nevi

The chief significance of the blue nevus is that its clinical appearance may suggest malignant change Careful attention to the history usually will reveal, however that there has been no noticeable change in the appearance such as occurs in nevi undergoing melanomatous change Characteristically the blue nevus is a smooth hairless, flat or slightly elevated lesion of slate blue color

Inasmuch as blue nevi rarely undergo melanomatous change their removal usually is unnecessary However if there is doubt as to the diagnosis or if the lesion is subject to trauma or if it is cosmetically objectionable removal is indicated If there is suspicion that melanoma may be present, chemosurgical excision without preliminary surgical removal is indicated. However, if the clinical diagnosis clearly is blue nevus the lesion may be removed by the most convenient method which often is excision and suture or excision and cauterization with dichloracetic acid.

Other Pigmented Lesions

Intraepidermal pigmented nevi melanosis and other pigmented lesions not containing nevus cells occasionally require removal either for cosmetic reasons or to rule out melanomatous or premelanomatous conditions. If there is any doubt as to whether or not the diagnosis is melanoma the lesion should be chemosurgically excised without preliminary surgical removal. Usually however the diagnosis is fairly obvious and treatment either by simple excision and cauterization with dichloracetic acid or excision and suture is sufficient. For example melanotic macules on the lip usually require no more than superficial excision and cauterization with dichloracetic acid. However a frozen section always is made to rule out junction nevus or melanoma.

Lentigo consists of brownish black or black macules which occur most often on the dorsa of the hands although they are not infrequent



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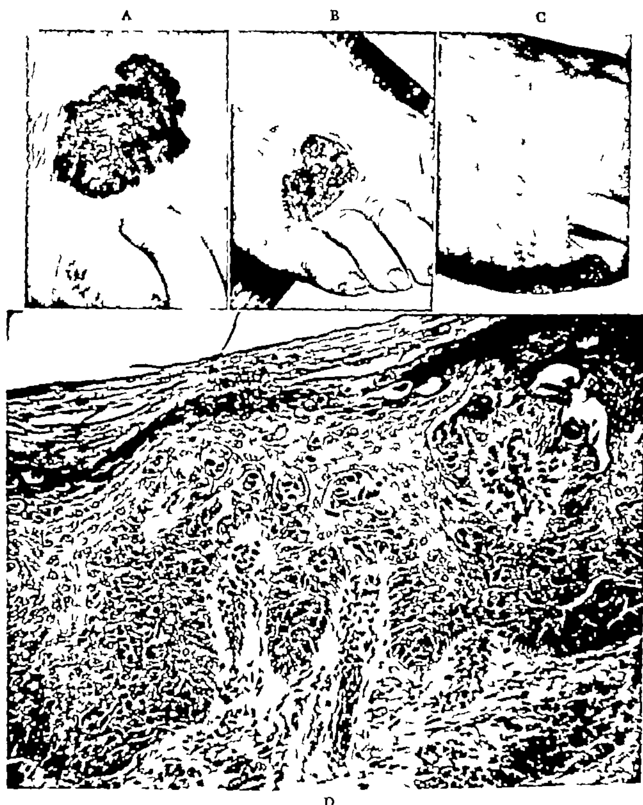


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in other exposed areas. Microscopically lentigines are characterized by acanthosis with the formation of thumb-like rete ridges. The pigment is largely in the basal layer of the epithelium. Rarely, these may develop into junction nevi and occasionally they develop into senile keratoses which may take on activity and eventuate in squamous cell carcinoma. Usually removal is unnecessary unless some growth occurs in which case excision and cauterization with dichloracetic acid is carried out.

CHAPTER 26

Tumors of Infectious Origin

TUMORS which depend on the presence of an infectious agent for their growth can not be considered to be true autonomous neoplasms. Nevertheless, their eradication usually depends upon the complete removal of the tumor along with its contained causative agent To assure complete removal of these lesions excision and cauterization with dichloracetic acid usually suffices especially if carried out under magnified vision, but the microscopic control of excision afforded by the chemosurgical technic occasionally may be desirable, particularly when there is a question of possible malignancy

Common Warts

Verrucae vulgares or common warts are infectious tumors produced by a filtrable virus. Unless they are removed completely they are likely to recur Therefore, the first requirement of a method of treatment is that it provide assurance of complete eradication. Also the method should spare the adjacent normal tissues so that the resulting scars are minimal. Furthermore, the treatment should not be too painful and, if possible, it should be carried out in one visit. All of these requirements are met by the following procedure by which warts may be excised under magnified vision.

Local anesthesia is accomplished by injection of procaine hydrochloride The grossly visible portion of the wart is excised in such a manner that a saucerized defect is produced. The resultant bleeding obscures the tissues and makes it difficult to see whether all of the wart has been removed. To stop the bleeding and render the wart tissue readily recognizable through a binocular loupe the surface of the saucerized wound is cauterized with dichloracetic acid This chemical turns the epithelial tissues white but the blood in each of the capillaries of the papillae is turned black. Thus the wart tissue presents a white surface sprinkled with black specks. Wherever any of this characteristic tissue remains another layer is excised and the surface again cauterized. This is repeated until all of the wart has been removed At the periphery the presence of wart may be manifested by thickening of the stratum spinosum and stratum granulosum The thickness of these layers is readily ascertained after cauterization of the surface with dichloracetic acid because these layers turn dead white while both the underlying dermis and the overlying stratum corneum presents a grayish appearance Excision and cauterization at the periphery also is repeated until the thickness of these layers appear normal. In some lesions, especially those around the fingernails the peripheral extension of the deeper portion of the wart may be appreciably wider than one would expect from the initial clinical appearance of the wart. It is probable that this peripheral extension is the most common source of recurrence after the removal of warts with methods that do not provide such accurate visual control of excision.

Since warts are autoinoculable and since the incubation period of the causative virus may be nearly a year it is desirable not only to remove the initial lesion but to have the patient report promptly if new lesions appear Only when there have been no new warts for a period of a year can one feel fairly certain that the virus no longer inhabits the skin. Incidentally the thorough cleansing of the surrounding skin and the application of a virucide such as zephiran solution 1 100 to the skin around a wart both before

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Common Warts

Verrucae vulgares or common warts are infectious tumors produced by a filtrable virus. Unless they are removed completely they are likely to recur Therefore the first requirement of a method of treatment is that it provide assurance of complete eradication. Also the method should spare the adjacent normal tissues so that the resulting scars are minimal Furthermore, the treatment should not be too painful and, if possible, it should be carried out in one visit. All of these requirements are met by the following procedure by which warts may be excised under magnified vision.

Local anesthesia is accomplished by injection of procaine hydrochloride The grossly visible portion of the wart is excised in such a manner that a saucerized defect is produced. The resultant bleeding obscures the tissues and makes it difficult to see whether all of the wart has been removed To stop the bleeding and render the wart tissue readily recognizable through a binocular loupe the surface of the saucerized wound is cauterized with dichloracetic acid This chemical turns the epithelial tissues white but the blood in each of the capillaries of the papillae is turned black. Thus the wart tissue presents a white surface sprinkled with black specks Wherever any of this characteristic tissue remains another layer is excised and the surface again cauterized. This is repeated until all of the wart has been removed. At the periphery the presence of wart may be manifested by thickening of the stratum spinosum and stratum granulosum. The thickness of these layers is readily ascertained after cauterization of the surface with dichloracetic acid because these layers turn dead white while both the underlying dermis and the overlying stratum corneum presents a grayish appearance. Excision and cauterization at the periphery also is repeated until the thickness of these layers appear normal In some lesions, especially those around the fingernails the peripheral extension of the deeper portion of the wart may be appreciably wider than one would expect from the initial clinical appearance of the wart. It is probable that this peripheral extension is the most common source of recurrence after the removal of warts with methods that do not provide such accurate visual control of excision.

Since warts are autoinoculable and since the incubation period of the causative virus may be nearly a year it is desirable not only to remove the initial lesion but to have the patient report promptly if new lesions appear Only when there have been no new warts for a period of a year can one feel fairly certain that the virus no longer inhabits the skin. Incidentally the thorough cleansing of the surrounding skin and the application of a viricide such as zephiran solution 1 100 to the skin around a wart both before

and after treatment are precautionary measures which may reduce the chances of autoinoculation through needle tracts or abrasions.

Occasionally there may be some doubt as to whether a lesion is a wart or whether it is a squamous cell papilloma or even a squamous cell carcinoma. In such cases a frozen section of the excised specimen should be made. The characteristic architecture of the wart usually is readily distinguishable from that of the precancerous and cancerous lesions the presence of vacuoles in the cells of the prickle and granular cell layers of many warts occasionally provides a helpful differential point.

Flat juvenile warts (verrucae planae juveniles) usually are superficial and require no more than superficial excision and cauterization with dichloracetic acid. If the warts are very small, only cauterization with dichloracetic acid is necessary. Filiform warts may be excised with a knife or scissors and the base cauterized with dichloracetic acid. Venereal warts (condyloma accuminata or verrucca accuminata) may be treated the same as common warts.

Using the technics described above 162 verrucae vulgares were removed from 126 patients with good results in all cases except for a few in which there were peripheral recurrences which required further treatment of the same type for complete eradication.

Plantar Warts

Because of their location on the heavily hornified plantar surface verrucae plantares have a different clinical appearance than warts elsewhere on the body. Often the papillated nature of the lesions is masked by an overlying callus which may be relatively smooth. Upon paring off the overlying callous tissue, however the underlying wart is manifested by the small vessels which occupy the center of most of the papillae. Some of the vessels may bleed upon being cut across but some of the cut vessels may appear as black specks owing to thrombosis. In the absence of these vessels in lesions which have received previous treatment it may be concluded that the lesion is a post treatment callus rather than a wart.

The treatment of plantar warts is essentially the same as that of warts in other locations. If there is any doubt as to the diagnosis, th is pared until the characteristic warty p with their contained vessels are encou Then, when the presence of a wart ha established, local infiltration with proc accomplished through a single point of tion which preferably is through the and less sensitive skin at the side of the at the bases of the toes. If the wart is o the nerves just proximal to the lesi blocked through a single point of injectio

The main body of the wart then is producing a saucerized depression. The ing is stopped by the application of d acetic acid. This whitens the tissues and ens the vessels which are readily visualize a magnifying glass, or preferably with a nifying loupe. The areas of wart thus vis again are excised and dichloracetic ac plied. This is repeated until no more p can be demonstrated. Then attention is d to the epidermis at the periphery of the at times some vessels may indicate the p of wart in this region but often the only tion is thickening of the epidermis. readily observed because the dichloracet quickly whitens the stratum spinosum stratum granulosum which layers stan from the underlying dermis and from th lying, more slowly penetrated stratum co Layers of epidermis are successively re until the thickness appears normal.

After completion of treatment a amount of petrolatum is applied. The may be left open or if desired, a sma dressing may be applied. Sometimes the becomes sufficiently tender and painf justify the use of a mild analgesic. If steri forms under the eschar the resultant d fort may be relieved by paring the edge defect and liberating the pus. The caut tissue usually is ready to separate in ten to teen days, although the time may be grea previous radiation treatment has been rec Mercurochrome is applied to the res wound which is kept covered with a dry ing If the granulation tissue reaches th level the dry dressing may stick to the w and in this event the use of scarlet red ment-impregnated gauze is preferred.

The wounds heal with flat scars which remain slightly hyperkeratotic for a few weeks and then become soft smooth and comfortable (Fig 183) Larger warts of the mosaic type are extremely large or unless there has been much tissue damage from previous radiation therapy Plastic repair may be required in rare instances of this nature. If there is any question



Fig 183 (A) *Plantar warts of seven years duration Cauterization with an acid had been ineffective.* (B) Granulation tissue after separation of cauterized tissue after seven days. (C) Healed lesions. There is no evidence of recurrence after eight years.

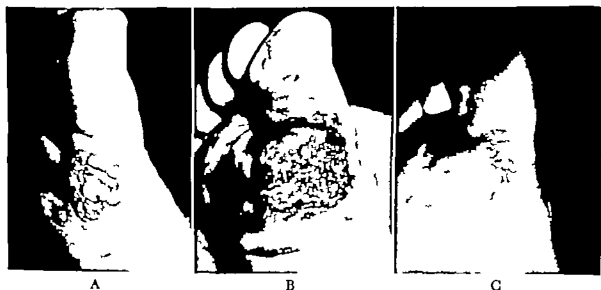


Fig 184 (A) Mosaic type of plantar wart. It had failed to respond to treatment with x rays and radium two years previously and fulgeration one year previously Three other warts were present on the plantar surface (B) Granulation tissue after separation of the cauterized tissue nine days later (C) Healed lesions. Three months later a small recurrent wart at the medial edge of the scar was removed. When this photo was taken one year after treatment the scar was soft, pliable and comfortable.

are treated in the same manner except of course, that a relatively large area may have to be removed (Fig 184) Usually it is unnecessary to remove much of the plantar fat pad hence the scars are satisfactory unless the lesions of malignancy the lesion should be studied microscopically Histologically the non invasive nature of the wart tissue usually is readily apparent in addition, the presence of vacuoles in the cytoplasm of the cells is pathognomonic. In

this series, only one cancer was observed to arise in a plantar wart this was a squamous cell carcinoma which appeared in a wart which had been present for nineteen years. This lesion was chemosurgically excised and there was no evidence of recurrence or metastasis after six years.

As with warts elsewhere there is always a possibility that more warts may form either at the edge of the scar (Fig 184) or elsewhere owing to the retention of wart virus in the skin. Accordingly the patient is instructed to return immediately if any new foci are noticed If the warts are detected early they may be removed very easily and conservatively sometimes they are so superficial that it is unnecessary to penetrate the full thickness of the epidermis.

In a series of fifty patients ninety four plantar warts have been removed by the technics described above. Over half of the lesions (54 3 per cent) were warts which had failed to respond to previous electrodesiccation, application of caustics, excision, roentgen rays or radium. All of the lesions eventually were eradicated except for those in two patients who had multiple mosaic warts which were not completely controlled when the r seen. It should be pointed out, several of the patients near or at a distance from the were readily controlled by the sa p ctically no recurrences have be

since close attention has been paid to the thickness of the epidermis at the periphery of the main body of the wart.

Post radiation calluses following the treatment of warts with roentgen rays or radium may be persistently troublesome and they often are erroneously believed to be recurrent warts. Since the hyperkeratotic mass causes irritation which in turn leads to more callus, treatment is aimed at breaking this vicious circle by repeated paring of the callus. This often can be done with a razor by the patient but there may be corn like central pegs of keratin which may require paring with a scalpel. Sometimes the lesion is cauterized with dichloracetic acid after completion of the paring The patient is requested to keep the callus pared and the skin slightly lubricated for as long as necessary for the tissue to approach normal. Often many months or even years may elapse before this occurs, particularly in patients who have received heavy doses of irradiation.

Molluscum Contagiosum

The infectious and autoinoculable nature of molluscum contagiosum accounts for the multi-



A

Fig 185 (A) Molluscum contagi hotomicrogr pecimen showing the character contagio

nl in m Character istic are sh white 1 s (Fig 185A) can be are com- 1 central

Lesions

and superficial portions of the lesion assume a peculiar expanded oval dyskeratotic appearance. These cells are known as molluscum bodies (Fig 185B)

The nodules may be removed very conservatively If small cauterization with dichloracetic acid is sufficient. If larger excision to the skin level under local anesthesia followed by cauterization with dichloracetic acid is necessary The extent of the whitish tissue of the nodule is readily visualized after cauterization and if excision is seen to be incomplete more tissue is excised and the lesion again cauterized The lesions tend to be very superficial therefore the scars following their removal are minimal

The patient should be instructed to return promptly if any new nodules are noticed. Several months must elapse before one can be fairly sure that the virus no longer is present in the skin. In one patient thirty six lesions were removed over a period of four months, but in the ensuing ten years no new lesions appeared

Granuloma Pyogenicum

This tumor is composed of a circumscribed mass of highly vascular granulation tissue. Inasmuch as the lesions do not tend to regress spontaneously their removal is indicated If the lesion is small, cauterization with dichloracetic acid and a small amount of zinc chloride fixative paste ordinarily is sufficient. If larger excision under local anesthesia followed by cauterization with dichloracetic acid is effective The soft spongy red granulation tissue should be removed to a level at which the firmer normal tissue is encountered If the epidermal edges are undermined the removal of the overhanging skin is advisable Ordinarily treatment may be very conservative hence the resultant scars are unnoticeable (Fig 186) In one patient with hemophilia a granulomatous mass which had arisen from an ingrown toenail had grown large because of hesitancy to attempt operative treatment in the presence of a hemorrhagic tendency The granuloma was removed chemosurgically without bleeding during excision because the blood was coagulated within the vessels by the fixative and without bleeding during separation of the final layer of fixed tissue because by that time the ends of the vessels had healed across. Recurrence of the ingrown toenail was prevented, as it has been in many cases, by tucking scarlet red ointment impregnated gauze under the edge of the nail. This not only served to keep the nail from contacting the soft tissues, but it also exerted a

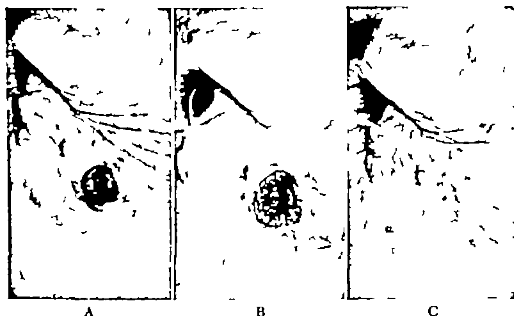


Fig. 186. (A) *Granuloma pyogenicum. The sudden appearance of a rapidly growing nodule in a scaly pigmented patch suggested the possibility of melanoma.* Therefore the lesion was excised chemosurgically (B) Granulation tissue after separation of final layer of fixed tissue (C) Healed lesion.

mild antiseptic action and promoted epithelization.

After removal of the granuloma the wound may be left open or covered with a dry dressing. After separation of the cauterized layer of tissue the wound may be painted with mercurochrome and a dry dressing applied. If there is a possibility of the dressing sticking scarlet red ointment impregnated gauze dressings are preferred.

By the methods described above, twen pyogenic granulomas have been removed healing in every case.

Other Tumors of Infectious Origi

Tumor like granulomas may be produc the causative organisms of tuberculosis, b mycosis, actinomycosis and certain chronic infections. These conditions are d sed in the section on infections.

CHAPTER 27

Precancerous Conditions

CANCER of the skin can be prevented to an appreciable degree in two ways first by the avoidance of undue exposure to carcinogenic agents and second by the removal of precancerous lesions

By far the most common carcinogenic agent is sunlight, or more specifically the band of ultraviolet rays between the wavelengths of 2,800 and 3,200 angstrom units This has been amply demonstrated by laboratory investigations, but long before these experiments the carcinogenic influence of sunlight was indicated by numerous clinical observations. For example keratoses and cancers are more common on the exposed skin than on the covered skin they are more common in blonds and reddish blonds than in brunettes and they are more common in farmers sailors and other outdoor workers than in indoor workers and finally they are more common in males than in females. The last point is illustrated by the fact that in the present series of 4 442 cancers on the exposed parts of the body 72.2 per cent were in males. The discrepancy is even greater for cancers of the ears (88.8 per cent in men) because women s ears usually are covered by their hair scarves or hats. Cancer of the lip is much more common in men (98.4 per cent) not only because of the greater exposure to sunlight but also because of the greater use of tobacco and the higher incidence of oral sepsis.

In general, persons who sunburn readily are most susceptible and they should be warned to protect their face and hands with hats, gloves and sunscreen lotions when long exposure is anticipated. Sunbathing of the other parts of the body usually need not be restricted since it is unlikely that the total amount of ultraviolet rays received in this way would reach carcinogenic levels. Since it is the cumulative dose over the life span that is effective in the development of precancerous and cancerous lesions in a given site the only areas about which one need be concerned are those that are daily exposed to some amount of radiation.

Other carcinogenic agents which nowdays only rarely are responsible for cutaneous cancer are pitch tars chimney soot, and arsenic (Fig 107) With the modern care of burns, cancers arising in burn scars are becoming rare as are those arising in varicose ulcers. Roentgen rays, radium and other radioactive materials continue to be a potential danger especially to physicians, dentists and others who are repeatedly exposed to the rays which have a cumulative effect. Naturally the more one can avoid these cancer producing factors the less is the likelihod of cancer

The second way in which external cancers may be prevented is by the removal of precancerous lesions of various kinds. This may be done by the technic outlined herewith

Senile Keratoses

By far the most frequent precursor of carcinoma of the skin is the senile keratosis. Perhaps a better term would be actinic keratosis because these lesions may appear before the age of thirty if the person has a light, reddish blond complexion and if exposure to sunlight is exceptionally heavy

Senile keratoses may be said to be "inactive" or "active" according to the amount of epithelial proliferation present. The inactive keratosis is characterized by very slightly thickened epidermis with adherent horny scales and possibly with some brownish pigmentation. The active keratosis is a more elevated lesion which ex

hibits more thickening of the epidermis, some degree of papillation and heavy horny scales which upon removal leave bleeding points. Often there is an inflammatory reaction and, as a result of trauma, the lesion may become partially ulcerated and covered with bloody crusts. The clinical distinction between inactive and active keratoses is useful because while the inactive lesion may be present for some time without proceeding to cancer the active keratosis is likely to undergo malignant change within a relatively few months. Hence, active keratoses should be removed immediately On the other hand inactive lesions may safely be let alone until they become active. However, the patient often wishes them removed for



Fig 187 (A) Senile keratosis which was active as evidenced by elevation and induration of the base, and by ulceration with crust formation. (B) Healed lesion after chemosurgical excision. Microscopically there were observed deep epidermal downgrowths under which there were dense infiltrations of small round cells.

cosmetic purposes. If he lives long enough it is likely that most inactive keratoses eventually would become active and finally become cancerous. Therefore, if the patient has a long life expectancy there is ample justification for removing inactive as well as active keratoses. Lentigenes, the flat, pigmented macules which commonly occur on the hands and face of elderly people need not be removed unless active keratosis formation supervenes.

If not too thick or active, keratoses may be removed most conveniently by the simple application of dichloracetic acid or a saturated solution of trichloracetic acid. Usually the keratin scales must be scraped off to allow the acid to penetrate to the bottom of the epidermis. It is convenient to keep a dull scalpel for scraping because the acid quickly damages the cutting edge of a sharp blade. The penetration of the acid to the prickle cell layer is signalled by whitening of the skin owing to coagulation of the proteins in the cells of this layer Hence, treatment should not be considered complete until the entire lesion turns white. It may be necessary to apply the acid and to scrape off the keratin several times if this layer is thick, hard and dry No anesthesia is necessary unless the area is large.

Keratoses which are thick, heavily keratinized and papillated are more rapidly treated by excision under local anesthesia followed by cauterization of the base with dichloracetic acid. Besides being rapid and painless this technic provides a specimen for frozen section which is important if there is any question of possible incipient carcinoma If malignancy is demonstrated microscopically zinc chloride fixative is applied and a layer of fixed tissue subsequently is excised for microscopic determination of the progress of removal.

Squamous cell papillomas and cutaneous horns may be considered forms of senile keratoses which have progressed a little further than usual in the degree of papillation or keratin scale formation. These lesions almost always are sectioned because they often undergo malignant change.

In a series of 633 senile keratoses treated by the technics described above, the different forms of keratoses occurred in the following order of frequency senile keratoses, 500 cases or 79 per cent squamous cell papillomas, 106 cases or 16 7 per cent and cutaneous horns, twenty-seven cases or 4.3 per cent. As regards proliferative activity a large majority of the keratoses were listed as "active" rather than "inactive." The results of treatment were uniformly satisfactory both as regards eradication of the lesions and as regards cosmetic results (Fig 187)

Arsenical Keratoses

Rarer now that potassium arsenite or Fowler's solution is less used arsenical keratoses are precancerous lesions that mainly

affect the palms and the soles where the keratin is thick enough to store carcinogenic amounts of trivalent arsenic for a prolonged period In these locations the keratoses tend to lead to squamous cell carcinoma unless they are removed. The same technics as outlined for senile keratoses are effective

Another type of cancer which may be caused by arsenic is the superficial basal cell carcinoma which most characteristically occurs on the trunk. As pointed out in the chapter on cancer of the trunk, there were three instances of this condition in patients who had received Fowler's solution for their psoriasis. Some of the carcinomas arose at the site of psoriatic lesions suggesting the possibility that there may have been retention of arsenic in the hyper keratotic patches, much as there is in the thick keratin of the palms and soles. However it would not be practical to remove the psoriatic lesions for the purpose of preventing cancer even though it is possible to remove small lesions without noticeable scarring by the application of dichloracetic acid.

Xeroderma Pigmentosum

This condition usually has its onset in infancy and is characterized by multiple keratoses and carcinomas which result from an abnormally great sensitivity to the ultraviolet rays of sunlight. The removal of the keratoses may be by cauterization with dichloracetic acid or by excision and cauterization. If cancer is suspected microscopic examination of the excised specimen is indicated and if this shows malignancy the neoplasm is removed chemosurgically Using these chemosurgical technics, one patient with xeroderma pigmentosum has had numerous keratoses and twenty seven carcinomas removed. At the age of twenty-one he is currently free of cancer (Fig. 34)

Another patient developed the atrophy scarring, hyperkeratosis and telangiectases of xeroderma pigmentosum during childhood but had no carcinomas until the age of twenty five when she developed a squamous cell carcinoma of the lower lip and three basal cell carcinomas of the face. Over a period of nine years she developed fifteen carcinomas of the face of these thirteen were basal cell carcinomas and two were squamous cell carcinomas These lesions in addition to numerous keratoses were removed chemosurgically and the patient was free of cancer when she died of other causes at the age of thirty seven This case is unusual in regard to the late onset of the carcinomas and in regard to the high proportion of basal cell carcinomas As a rule squamous cell carcinomas predominate in this disease.

Seborrheic Keratoses

These lesions which also are termed basal cell papillomas or verrucae senilis occur most frequently on the temples eyelids back and chest but may form almost anywhere on the skin. Characteristically the lesions are superficial elevated placques, brownish black or yellowish-brown in color with a papillated surface covered with greasy scales Only rarely do seborrheic keratoses lead to cancer and when they do the carcinoma usually is of the basal rather than the squamous cell type Hence they are most often removed for cosmetic reasons rather than for the prevention of cancer However in cases in which there is active growth and there is a question of malignancy removal and microscopic study of the specimen is indicated.



Fig 188 (A) Seborrheic keratosis which had been construed as possible melanoma by the referring physician. (B) Healed lesion after chemosurgical excision.

If there is any question of melanoma the growth should be removed by the chemosurgical technic (Fig 188) Otherwise those that are not much elevated may be cauterized with

dichloracetic acid The greasy scales on the surface and the keratin cysts in the superficial part of the lesion are scraped off with a dull scalpel and the acid is reapplied until the entire lesion turns white. Lesions which are elevated are more readily removed by superficial excision to the skin level under local anesthesia followed by cauterization of the base with dichloracetic acid (Fig 189) The exact extent



A B C

Fig 189 (A) Seborrheic keratosis. (B) Granulation tissue after excision and cauterization. (C) Healed lesion.

of the keratosis is readily visualized grossly by this technic. The remaining layer of cauterized tissue may be left uncovered or if desired, it may be covered with a dry dressing After the slough separates in a week or two the lesion may be healed but if it is not mercurochrome may be applied to provide a protective crust till healing is complete. If the lesion is within the hairline, the level of destruction often need not be deep enough to destroy the germinal elements at the bottom of the hair follicle in this way bald spots may be avoided.

Using these technics more than 500 seborrheic keratoses have been removed with uniformly satisfactory results as regards both permanency of eradication and cosmetic results.

Bowen's Disease

Although now considered to be squamous cell carcinoma in situ, Bowen's disease originally was described as a precancerous dermatosis. The slightly elevated, indurated, scaly crusted, erythematous placques usually are single but may be multiple. They may readily be mistaken for superficial erythematous basal cell carcinomas. Histologically there is extreme irregularity of the acanthotic epidermal structure and there are scattered multinucleated, and vacuolated cells. Although the lesions clinically appear to be well circumscribed there occasionally is peripheral extension for several millimeters beyond the apparent edge. Therefore, the entire periphery of each lesion always is checked microscopically by means of the chemosurgical technic.

Nevi

Carcinoma in contrast with melanoma only rarely arises in association with nevi. Thus, of 2 483 basal cell carcinomas only three arose in nevi and of 1 734 squamous cell carcinomas only one arose in a nevus. All of the carcinomas associated with nevi arose in intradermal nevi while all of the melanomas associated with nevi arose in junctional nevi.

In consideration of the rarity of carcinomatous change in intradermal nevi they need not be removed as a cancer preventive measure unless they are subject to trauma or unless they start to grow change color or become ulcerated. Under these circumstances the nevus should be excised, the base cauterized with dichloracetic acid and a frozen section made to determine whether or not malignant change has occurred If malignancy is found the neoplasm should be removed by the chemosurgical technic in order that complete eradication may be assured by microscopic means.

Leukoplakia, Keratoses and Chronic Ulcers of the Lips

These conditions are considered together not only because they are about equal in their tendency to undergo carcinomatous change but also because they not infrequently occur together in the same patient. Moreover the three lesions may be removed by the same technic

Leukoplakia is characterized by a whitish patch which usually affects the moist portion of the lip nearest the oral mucosa. Often but by no means always, the patient smokes hence the synonym, "smoker's patch. Often poor oral hygiene also seems to be a consideration but sometimes no definite causative factor is apparent. There is great variation in the thickness of the patches hence the lesions may vary in appearance from a flat, barely perceptible grayish macule to an elevated thick dead white placque (Fig 190) The former occasionally may disappear upon cessation of smoking and improvement in oral hygiene but the thicker lesions rarely do Since well developed leukoplakia has a strong tendency to lead to squamous cell carcinoma it should be removed without delay If there are concomitant lesions on the oral mucosa they should be treated in the same way

Keratoses tend to occur on the dry portion of the lip nearest the skin (Fig 191) Often a line of hyperkeratotic mucosa extends from one side of the lower lip to the other this usually is 2 or 3 mm. posterior to the mucocutaneous junction. Exposure to sun and wind definitely increases the incidence of labial keratoses hence they are most common in outdoor workers such as farmers and telephone linemen. Other etiologic factors are mechanical trauma, as by the sticking of cigaret paper and chemical irritation as by tar from tobacco or other sources.



Fig 190 (A) Leukoplakia which extended posteriorly into the oral mucosa of the left half of the lower lip (B) Healed lesion after chemosurgical excision.



Fig. 191 (A) Keratosis with ulceration and crusting (B) Healed lesion after chemosurgical excision.

The keratosis may vary from a barely perceptible area of scaliness to a thick, horny adherent scale. When there is definite thickening, the lesion is strongly precancerous and it should be removed without delay

Ulcers and fissures of the lips are so often associated with leukoplakia and keratoses that they may be considered to be complications of leukoplakia or keratosis rather than being pre cancerous entities in themselves. Ulcers of infectious origin such as cold sores and Vincent's angina may be differentiated from precancerous ulcers by their characteristic clinical features and by their tendency to be of short duration. Any ulcer or fissure that persists for several weeks is likely to be a precancerous lesion and should be removed

The method of removal depends on the thickness of the leukoplakia, keratosis or the ulcerated lesion. If they are thin superficial and only slightly indurated, the simplest treatment is cauterization with dichloracetic acid The keratinaceous material may have to be scraped off several times between applications of the acid in order to allow complete penetration which is signalled by whitening of the lesion. On the other hand, if the lesion is thick and indurated the quickest and least painful treatment is excision under local anesthesia, followed by cauterization of the base with dichloracetic acid. Importantly this also provides a specimen for a frozen section which is useful if there is any doubt regarding possible malignant change. Regardless of which method is used, the layer of cauterized tissue separates spontaneously in three to five days. Mercurochrome then is applied daily until healing is complete. No dressings are necessary Even if the process involves a linear area across the entire lip the wound heals well with scars that are unnoticeable.

Using these methods ninety patients with leukoplakia and 136 with keratosis of the lip were treated with uniformly satisfactory results. In a few of the patients further treatment was required because of new precancerous lesions which subsequently appeared elsewhere on the lip However even if the patient should develop two or three more precancerous lesions, the relative ease of removal by the above described methods makes this course preferable to a more radical procedure such as excision of the labial mucosa followed by replacement by a sliding flap of oral mucosa. A number of ulcers and fissures were removed but since in most cases these lesions were complications of keratoses they were listed as such.

In six patients there were ulcers which resulted from previous irradiation of lip cancers with roentgen or radium rays. In all of the cases the wounds healed following chemosurgical removal of the damaged tissues but in some cases the scars were more or less depressed and atrophic as a result of the radiation. In the cases in which there was a question of residual malignancy, frozen sections provided a definite microscopic diagnosis.

Miscellaneous lesions which were removed from the lips either for the purpose of ruling out malignancy or for the purpose of eliminating a possible precancerous lesion were the following one granuloma pyogenicum, one discoid lupus erythematosus one sarcoid, eight melanotic patches, three intradermal nevi, three sebaceous cysts, two traumatic implantation cysts, and one fibroma. The wounds healed uneventfully and permanently in every case.

Epidermal and Sebaceous Cysts

Inasmuch as squamous cell carcinoma occasionally may arise in epidermal or sebaceous cysts (Fig 14) the removal of these lesions may be considered to be a cancer-preventive measure. This is especially true if the wens are large, infected, ulcerated, subject to trauma or if they are of very long standing There are several ways in which these cysts may be removed.

Often the simplest method of removal is enucleation and suture after anesthetization of the area with procaine This method is especially suited to lesions on the scalp for it produces no bald spot, and it often is the method of choice in other areas as well Smaller cysts often may be shelled out intact but there is no objection to incising larger lesions and removing the cheesy contents if one is careful to avoid implantation of fragments of the cyst wall in the wound. The collapsed wall of the cyst may be removed through a much smaller incision than otherwise would be possible. If there has been an inflammatory reaction from

infection, trauma or ulceration the lining may be so adherent that it cannot be shelled out in that case it has to be dissected out with care to avoid leaving any fragments of the cyst wall

Another method of removal is to unroof the cyst, remove the contents and cauterize the denuded tissues at the periphery with dichloracetic acid. The epidermis of the floor of the cyst is not cauterized and it gradually is replaced by normal skin.

A third method is to cauterize the apex of the cyst with dichloracetic acid and zinc chloride fixative paste After a few minutes the cyst may be opened, the contents scooped out and the lining cauterized with dichloracetic acid The cyst wall sloughs out in a week or so and no further attention is necessary except, perhaps the application of mercurochrome and a dry dressing for a few days. This technic occasionally is useful for cysts with heavy scarring from infection or previous excision because it allows sure eradication of the cyst wall including possible outpouchings in the scar tissue

Using the technics described above fifty four epidermal and sebaceous cysts were removed without any recurrence. Although the lining of each of the cysts was thoroughly examined in good light and often by microscopic sections no instance of cancer was found other than the one illustrated in Figure 14 The proportion of epidermal to sebaceous cysts was approximately 1 4 but since a few were not examined microscopically the ratio is not exact. The wall of the epidermal cyst with its squamous epithelium desquamating horny laminations and intercellular bridges, usually are readily differentiated microscopically from the sebaceous cyst with its relatively unstratified epithelium sebaceous detritus vacuolated cells and its lack of intercellular bridges.

Although not known to have precancerous potentialities, a number of cysts of other types also have been treated with similar methods. The so-called "synovial cysts" which most commonly occur over the interphalangeal joints of the fingers are really mucinous degeneration cysts and they have been discussed along with tumors of mesodermal origin (Chapter 23) Cysts such as those that form in the glands of the eyelids and mammary nipples and those that form in the mucous glands of the lips and oral mucosa have been treated similarly as have various epithelial inclusion cysts of either traumatic or developmental origin. Cysts in which infection plays an important part include pilonidal cysts and hidrosadenitis suppurativa chronica which conditions are described in the section on infections.

Chronic Ulcers

Regardless of whether they originate on the basis of burn scar varicose dermatitis or other abnormality ulcers which persist over a period of years may lead to cancer Hence their removal is an effective cancer preventive measure

As was pointed out in previous chapters a number of squamous cell carcinomas had their origin in burn scars (Figs. 12, 104 and 109) Usually the neoplasms arose in the vicinity of ulcers which were the result of impairment of the blood supply by the underlying dense scar tissue With the modern treatment of burns such dense scars and resultant ulcers ordinarily should not develop but if they do they should not be allowed to persist. In some cases the chemosurgical removal of the infected, avascular tissue in the region of the ulcer will expose tissues with sufficient vascularity to allow prompt epithelization. However if the ulcer is very large excision and grafting often is preferred in order to minimize the further formation of scar tissue Varicose ulcers present much the same problem and the treatment is essentially the same except that attention to the causative varicose veins also is indicated.

Other chronic ulcers whether they arise from trauma (Fig 108) infection, vascular impairment or other cause should be considered as precancerous lesions and appropriate steps taken to eliminate them.

Radiation Dermatitis

Skin which has been exposed to large doses of roentgen or radium rays is predisposed to cancer The most common type of cancer from radiation is squamous cell carcinoma but occasionally basal cell carcinoma or sarcoma may result. Of the total of 1 070 squamous cell carcinomas observed in the Chemosurgery Clinic, fifty-eight (5 2 per cent) occurred in areas of

radiodermatitis while of the total of 2,544 basal cell carcinomas seventy-eight (3 1 per cent) developed in radiated skin. Sarcoma was observed in irradiated skin in two cases.

If the radiation dermatitis affects a large area, as for example, a large part of the face which has been irradiated for hypertrichosis, acne or eczema it usually is not feasible to remove all of the damaged skin. It is practical however to remove the keratoses and ulcers which commonly precede the development of cancer Keratoses, if they are superficial and have little proliferative tendency can readily be removed by cauterization with dichloracetic acid. If the bases of the keratoses become raised, indurated and elevated, however, it is safer to remove the lesions for microscopic examination for possible early malignancy This is most easily done by infiltrating the area with procaine, excising the lesion at a level slightly below the skin surface and cauterizing with dichloracetic acid If the microscopic section reveals incipient carcinoma the excision is completed under microscopic visualization by means of the chemosurgical method

Radiation ulcers and fissures may result from minor abrasions of the atrophic poorly nourished epidermis overlying the more densely scarred areas. These ulcers may be painful and persistent for years at a time and eventually they may lead to cancer Conservative treatment by the application of mercurochrome to provide a protective antiseptic crust may be tried but if the ulcer does not heal promptly it should be removed.

Ulcerated areas may be excised under local anesthesia and the base cauterized with dichloracetic acid or they may be chemosurgically removed by the application of zinc chloride fixative and subsequent excision In some cases it may be useful to microscopically examine the tissues at a given level to determine the amount of endarteritis scarring avascularity and degeneration because these criteria are helpful in determining how deeply the tissues should be removed to assure prompt epithelization. Sometimes several layers are chemosurgically excised before sufficiently well vascularized tissues are encountered. If healthy tissues are present the fixed tissue separates promptly revealing well vascularized granulation tissue which supports rapid epithelization On the other hand if the tissue is of borderline viability the fixed tissue remains adherent for an excessively long time and when it finally has been removed the scanty granulation tissue is pale and the surface is covered by a grayish membrane. When this occurs more tissue may have to be removed in order to reach a sufficiently well vascularized level or the entire area may be excised and grafts or flaps applied.

If there are tendons, bone or other solid structures in the base of a radiation ulcer they too may be chemosurgically excised. Necrotic bone often has a honeycombed, avascular appearance that allows ready differentiation from normal bone by gross visualization. If a line of demarcation already has formed the bone may be grasped with the rongeur and removed by a gentle rocking motion. If the bone remains adherent, however it may be fixed with the zinc chloride fixative and then removed by rongeur or chisel to the level of viable bone. As a result of the previous irradiation, subsequent separation of the final layer of chemically fixed bone may be delayed beyond the normal three week period but eventually a line of demarcation will form, perhaps after several weeks or even months.

Other relatively solid structures such as tendons, fascia, aponeuroses and cartilage also may have to be dissected out to allow the formation of adequate granulation tissue.

Using these methods, seventy-three patients with radiation sequelae were treated with satisfactory healing in all but a few patients. There were 14 patients with deep-seated radiation ulcers over the sacrum. These were the result of roentgen therapy of carcinoma of the cervix. With one exception all of the lesions were cleaned up and healing progressed almost, if not entirely, to completion (Fig 192) In these cases there was such profound damage to the deep tissues that the final stages of healing were delayed with resultant excessive scar formation which in turn tended to obstruct healing The placement of grafts as soon as good granulation tissue formed would have allowed more prompt and complete closure. In the one unsuccessfully treated patient the tissue was so

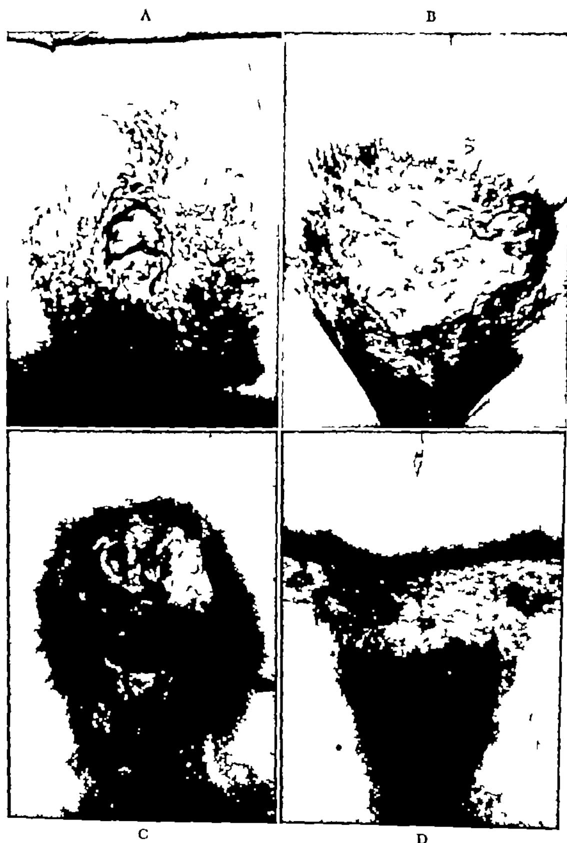


Fig. 192 (A) and (B) Ulcers over the sacrum and lower abdomen following roentgen therapy of carcinoma of the cervix. (C) and (D) Nearly healed lesions after chemosurgical excision. Because of radionecrosis of the bone it was necessary to remove the entire coccyx and a layer of the sacrum.

poorly vascularized that the fixed tissue failed to separate within a reasonable time. Therefore the entire area was excised by Dr E. R. Schmidt and following closure with a sliding flap the lesion healed without further difficulty This case illustrates the fact that when the radionecrosis has not involved the sacrum and coccyx it is possible to shorten the healing time by excision and plastic repair of the defect. However when the sacrum and coccyx have been involved as in the case illustrated in Figure 192 adequate surgical removal may not pair However when only moderate doses of irradiation have been received, prompt healing is the rule as has been observed in other patients who had received postoperative roentgen therapy but who had had recurrent nodules that were removed chemosurgically

Radiation keratoses and ulcers following roentgen treatment of carcinoma of the nose and ear may result in keratoses and ulcers that are particularly intractable because of the involvement of the cartilage. The chemosurgical excision of the damaged tissues often can be quite conservative and although the scar may remain depressed because of the atrophy from the irradiation the cosmetic result usually is satisfactory (Fig 193) An additional advantage of the chemosurgical method is that if any residual cancer is present in the lesion it will be detected and eradicated by the microscopically controlled technic (Fig 67)

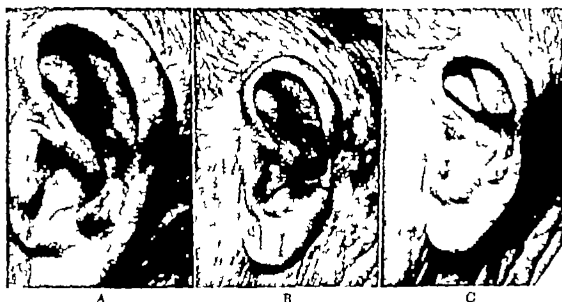


Fig 193 (A) Keratosis, ulceration and atrophy from two courses of roentgen therapy received for carcinoma ten years and one year previously (B) Granulation tissue after chemosurgical excision. This procedure not only allowed microscopic determination of the level at which vascularity was adequate but also ruled out possible residual malignancy (C) Healed lesion.

be feasible and certainly the wound would be grossly contaminated. In such a situation the chemosurgical technic may be useful not only because the fixation of the tissues facilitates accurate gross visual determination of the extent of the radionecrosis but also because by the time the fixed tissue is ready to separate the tissue spaces are closed and infection-resistant granulation tissue has formed

Radiation ulcers following roentgen treatment of carcinoma of the breast were removed in four cases, but the underlying tissues were so severely damaged in two patients that the wounds were excessively slow to clean up and heal. Perhaps the latter two patients would have done better with excision and plastic re-

In cases in which the induration, infection and ulceration are suggestive of residual carcinoma the chemosurgical method with its microscopic guidance of excision not only serves to demonstrate the absence of carcinoma but at the same time it eliminates the damaged tissue so that the lesion may heal (Fig 194)

The above described technics have been used

for the treatment of radiation keratoses and ulcers on practically every part of the body surface but since the methods used and the results obtained are similar for all they are not described and illustrated individually However since radiation sequelae as they occur on the hands of physicians and dentists constitute a special type of situation they will be accorded individual attention.

Radiation dermatitis in physicians and dentists exhibits characteristic localization patterns on the hands and fingers. Physicians tend to develop radiation sequelae on the backs of the hands and fingers because they receive most of their exposure while carrying out fluoroscopic procedures such as the setting of fractures or the removal of foreign bodies. Dentists on the other hand tend to develop their lesions on the thumb the middle finger and the base of the index finger because these areas are in the x ray beam while they are holding dental films in the mouths of their patients.[44] The tip of the index finger is practically always spared because of the filtration afforded by the teeth, alveolar bone and the metal foil on the back of the film.

As is pointed out in the chapter on carcinoma of the extremities physicians and dentists have in common a potent economic reason to preserve the function of their fingers To this end they should first of all, resolve strictly to avoid the roentgen beam unless their hands are well shielded by protective gloves. Particularly if they already show signs of radiation effect such as beginning atrophy telangiectasis and scaliness they should realize the great danger of the cumulative effects of further irradiation. Excessive sunlight or ultraviolet irradiation also should be avoided because the effects of these rays are additive to those of x rays and radium.

If keratoses already have developed they should be removed whenever they show any evidence of proliferative activity Removal is readily accomplished under local anesthesia by simple excision and cauterization with dichloracetic acid. A frozen section should be made to rule out possible early malignant change which if present, would call for chemosurgical excision. Small inactive keratoses may be kept pared or sanded or they may safely be removed by cauterization with dichloracetic acid. Lubrication of the skin with lanolin or similar product is advisable in order to replace the secretion of the sebaceous glands which have been damaged by the radiation. Superfatted soap reduces the drying from frequent washing

If small fissures or ulcers appear on the hands

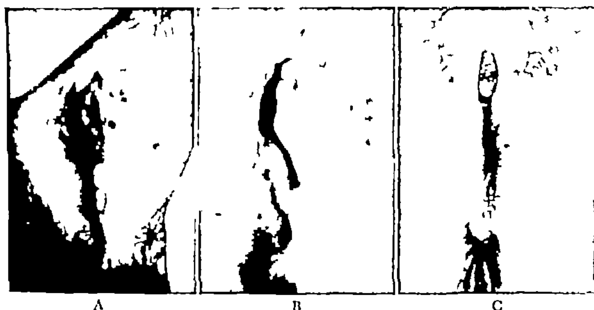


Fig. 194 (A) Radiation ulcer in region of clitoris. The painful ulcer had persisted for a year during which time three courses of radon seed therapy totalling 2 775 millicurie hours were received for squamous cell carcinoma of grade 1 malignancy (B) Granulation tissue after chemosurgical excision. No carcinoma was present. (C) Healed lesion. Note the atrophy from the radiation.

or fingers they may heal if the denuded area is kept covered by a protective crust formed by the application of a 10 per cent aqueous solution of mercurochrome. Stronger antiseptics such as iodine and alcoholic solutions should be avoided. If the lesion is large or if it is a fissure in the bend of a finger where the constant motion may deter healing unless the wound is kept lubricated, a preparation such as scarlet red ointment impregnated gauze is useful. Excessive amounts of ointments should be avoided because of the maceration and dermatitis they may produce. Larger fissures and ulcers which persistently fail to heal should be excised and *the area cauterized with dichloracetic acid.* The specimen should be examined microscopically to rule out cancer. Following excision of such lesions the cauterized tissue separates after a period of one to several weeks; the greater the amount of radiation received by the tissues the slower will the tissues separate. Either the use of mercurochrome with or without a dry dressing or the use of scarlet red gauze will promote prompt healing of the wound.

With the use of this conservative type of care the skin often will slowly improve (Fig 97). Even badly fissured nails may gradually get better (Fig 99). However the damage to the tissues is permanent and continued care must be exercised to avoid trauma, irritation or other adverse influences, not only for the purpose of keeping the hands functional but also to reduce the likelihood of malignant change.

Occasionally the degree of atrophy and scarring may be so great that excision and grafting may be indicated. If the underlying bone is severely involved, amputation of fingers or parts of the hand may be necessary.

Emphasis should be placed on the education of medical and dental students regarding the importance of avoiding ionizing radiations. It should be stressed that the effects of repeated exposures to radiation are cumulative and that chronic sequelae may not appear for ten or fifteen years after the main exposure. Incidentally this warning also must repeatedly be given to workers in the new field of atomic energy because the effects of these radiations are essentially the same as those produced by roentgen and radium rays.



Fig 195 (A) Squamous cell carcinoma, grade 2, arising in *lupus vulgaris* which had persisted for twenty years despite intensive roentgen, radium and ultraviolet therapy. The patient was a negro. (B) Granulation tissue after chemosurgical excision. (C) Healed lesion. There was no recurrence after six years.

Lupus Erythematosus, Discoid Type

This chronic disease, which is characterized by reddish or violaceous placques, occurs most commonly *on the nose, cheeks ears, scalp and lips.* The surface often is hyperkeratotic ex-

pecially at the openings of the hair follicles which usually are filled with horny plugs The dermis often is hyperemic and there is a low grade inflammatory infiltrate The disease may persist for years or it may partially or completely regress forming atrophic scars. In old lesions carcinoma occasionally develops. In the present series of cases of chemosurgically excised cancers there were four squamous cell carcinomas and one basal cell carcinoma which arose in association with patches of discoid lupus erythematosus

In view of the benign nature of discoid lupus erythematosus and the rarity of associated malignancy routine chemical cauterization of the lesions is not indicated. However, in patients whose lesions persist for a long time despite systemic and conservative local treatment the removal of patches under 2 cm. in diameter is justifiable as a cancer preventive measure. Removal may be accomplished by any of three methods (1) chemosurgical excision (2) excision under local anesthesia followed by cauterization with dichloracetic acid or (3) cauterization with dichloracetic acid The first two methods are used for thicker placques while the last method is used for the more superficial lesions Using these technics nineteen patients with one or more lesions were treated Of these, eight patients had no recurrence or new lesions after periods of one to five years two patients required further chemosurgical treatment before the disease was controlled two patients were reported to have developed recurrent or new lesions which were not treated and six patients were lost from observation Since the lesions were removed quite conservatively the cosmetic results in general were satisfactory

Lupus Vulgaris

This is a chronic infectious granuloma caused by the tubercle bacillus. With the possible exception of gumma it is the only infectious granuloma with an appreciable tendency to undergo malignant change In some cases the cancer may arise in untreated lesions, but usually there is the added carcinogenic effect of roentgen and ultraviolet therapy (Fig 195)

The chemosurgical treatment of lupus vulgaris is considered in the chapter on infectious granulomas.

PART III

GANGRENOUS CONDITIONS

CHAPTER 28

Gangrene of the Extremities

THE idea of using the chemosurgical technic for the conservative amputation of gangrenous parts was suggested by the excellent healing of the wounds resulting from the chemosurgical excision of cancers.[44] It was noticed that the tissues which had been killed by zinc chloride separated cleanly in approximately *one* week exposing well vascularized, infection-resistant granulation tissue which supported rapid epithelization and led to healing with remarkably soft, smooth healthy scars. The supposition that this excellent healing might be valuable in the treatment of gangrene a condition in which the capacity for healing is notoriously impaired has been borne out by the results of the chemosurgical amputation of 276 gangrenous lesions of the extremities of 248 patients. The different types of gangrene and the number of lesions of each type were as follows diabetic gangrene, 188 arteriosclerotic gangrene, sixty four frostbite gangrene, eleven Buerger's disease with gangrene, seven arterial embolism with gangrene, three femoral thrombosis with gangrene, two Raynaud's disease, with gangrene, one.

Technic

The essential steps of the chemosurgical technic for the amputation of gangrenous parts are first, the chemical fixation of the gangrenous part by means of zinc chloride and second, the excision of all except a thin layer of the chemically fixed tissue. This process is repeated until the desired level of amputation is reached The thin final layer of fixed tissue then is left in place until a well-defined line of demarcation has formed. Although the technic is essentially simple attention must be paid to a number of details in order to bring about optimal conditions for healing

Until recently no attempt was made to surgically amputate the bulk of the involved gangrenous part prior to the institution of chemosurgical treatment Hence the technic as it was used prior to this innovation is described as follows Following the administration of a suitable analgesic such as morphine sulphate ⅙ grain (10 mg.) the first step is the application of a keratolytic such as dichloracetic acid to the skin overlying the tissues to be removed Where the horny layer is thick, a number of applications of the acid alternating with repeated scraping with a dull scalpel are required before the layer is penetrated as indicated by whitening of the skin. Then the zinc chloride fixative paste (Z-108a) is applied in a depth of from 1 to 4 mm. depending upon the amount of penetration desired and upon extraneous factors affecting penetration such as the degree of circulatory impairment and the amount of inflammatory reaction and exudation The applied fixative then is covered with a layer of cotton which in turn is covered with another layer of cotton on which petrolatum is spread in order to secure an air tight closure. The dressing is fastened in place with adhesive tape or roller bandages.

After an interval of several hours, usually twenty-four the bulk of the chemically fixed tissue is excised with a scalpel. If the gangrenous part is a toe or a finger the fixation usually is sufficient to permit removal of most of the digit. The bone is clipped off with a rongeur or bone cutter After this first excision the amputation usually is not yet at the desired level and reapplication of the fixative to part or all of the area is required. The object is to obtain a flat saucerized wound (Fig 196B)

There should not be excessive protrusion of tissue in the center nor should there be excessive excavation or undercutting of the edges.

The final level of amputation depends upon the depth to which the gangrenous process extends. Often the gangrenous tracts extend considerably farther than the external appearance of the part would suggest. The fixed gangrenous tissue usually is relatively soft in consistency and dark in color hence, it is readily distinguishable from the fixed nongangrenous tissue which is firm and grayish white Often the gangrenous area is so soft that an applicator readily sinks into it in contrast with the surrounding fixed tissue which firmly resists such pressure. As long as gangrenous tissue is present the process of fixation and excision is repeated. Microscopic sections of the tissues at the level of amputation reveals the proportion of thrombotic vessels and the presence of degenerative changes in the fibrous tissues. This information is helpful in determining whether amputation at this level is likely to be successful.

The removal of the free portion of the toes may be carried out rapidly but when the distal part of the metatarsals are being amputated the speed of removal must be reduced in order that fixation is not inadvertently carried into the region of the metatarsophalangeal joint of the adjacent uninvolved toe. When the great toe is being amputated through the distal end of the metatarsal, the sesamoid bones are removed as are all of the joint structures.

When healthy tissue is present throughout and when a favorable level of amputation has been reached treatment is discontinued. The remaining thin layer of fixed tissue is covered with double thickness petrolatum gauze which is held in place by a gauze-covered cotton dressing

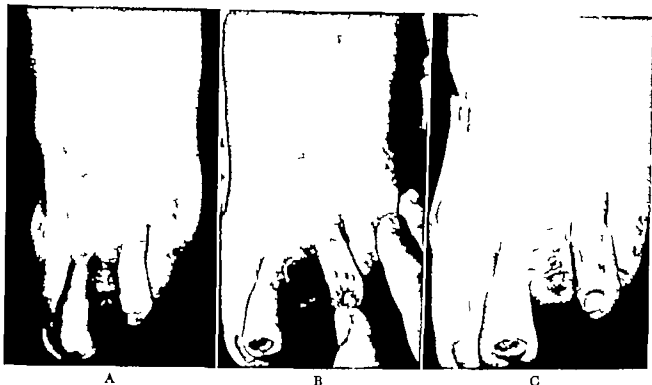


Fig 196 (A) Diabetic gangrene (B) Granulation tissue twelve days later The toe was chemosurgically amputated through the middle of the proximal phalanx. (C) Healed lesion two months later Epithelization was complete by thirty two days and the patient was ambulatory throughout.

After an interval of seven to fourteen days, a cleft forms between the fixed and unfixed tissue. The fixed tissue then can be removed by snipping with sharp-pointed scissors any adherent strands of tissue such as tendons, nerves and vessels. By this time granulation tissue has formed The fixed bone usually requires another week or two to become sufficiently demarcated from the unfixed bone so that it will separate readily when grasped with a rongeur and loos-

ened by means of a rocking motion. The bone thus exposed ordinarily bleeds freely and within a day or two granulations form on the surface. During separation of the fixed tissue and during healing sterile precautions are used.

Epithelization is promoted by the use of scarlet red ointment impregnated gauze dressings. The lesions heal with well vascularized, pliable scars (Fig 196C) The patient may remain ambulatory during treatment and during healing if the circulation is good and if the wound is not on the bottom of the foot. In the presence of wounds on or bordering on the plantar surface the patient should not step on the foot but should get around on crutches until epithelization is complete or nearly so. Otherwise the motion of the thick skin with each step tends to sever the delicate new epithelium from the granulation tissue producing a punched-out ulcer and causing delayed healing In patients with borderline circulation bed rest with the foot at the level of the heart is indicated during the period of healing Orthopedic appliances and special shoes are fitted as needed to avoid undue pressure on certain points of the deformed foot.

The choice of the level of amputation also is affected by factors other than the extent of the gangrene. If the gangrene extends to the level of an interphalangeal or metatarsophalangeal joint, it is advisable to carry fixation into the body of the bone proximal to the joint in order that complications in healing will not result from the failure of granulation tissues to form on the exposed joint structures Another factor which affects the level of amputation is the efficiency of the circulation of the part. For example if the circulation is not quite adequate at the level of the middle of the proximal phalanx, the amputation may be carried out through the distal third of the corresponding metatarsal at which level the vascularity may be adequate.

In patients in whom the efficiency of the circulation and the reactivity of the tissues are severely impaired the final layer of fixed tissue may fail to separate or it may do so very slowly (Fig 197) This delayed response in turn may lead to infection and extension of the gangrene Ordinarily if separation is not fairly well under way by ten days after completion of the chemosurgical amputation it may be concluded that healing is not likely to occur at that level. In such cases amputation at a higher level ordinarily is recommended although in some borderline cases another week or two may be allowed before a decision is made

A trial amputation followed by a waiting period of ten days may be thought of as a therapeutic test. Usually this procedure provides a more definite answer as to the possibility of successful conservative amputation than can be obtained by any of the various circulatory tests. If the outcome is unfavorable, nothing is lost as a result of the test except the ten days or two weeks. Moreover this loss of time often is counterbalanced by the improved general condition which results from the removal of the infected gangrenous tissue. In diabetics particularly the fever often subsides and the insulin requirement becomes stabilized at a lower level so that the patient becomes a better operative risk if a higher amputation of the extremity proves necessary



Fig 197 Diabetic gangrene with poor prognosis for healing at a conservative level. The pulsations of the popliteal artery were weak and those of the dorsalis pedis and posterior tibial arteries were absent. There was a sudden temperature change above the ankle the foot was cool and had a waxy pallor Histamine wheals were minimal below the knee and absent on the foot. There was no inflammatory reaction to the gangrenous tissu and the line of demarcation was not sharp. Despite the poor outlook the toe was chemosurgically amputated as a therapeutic test. After thirteen days the final layer of fixed tissue was firmly adherent Therefore, a midthigh amputation was carried out by Dr K. E. Lemmer with prompt healing

Although the above-described method of chemosurgical amputation was used with a

large measure of success over a period of seventeen years, the prospect of saving time and reducing the discomfort was offered by the preliminary surgical amputation of the main portion of the gangrenous part prior to the institution of chemosurgery. As yet, however, there is no assurance that this innovation will be without disadvantages. For example, it is possible that the injection of procaine prior to the initial amputation may tend to reduce the blood supply and the reactivity of the tissues in the region of the amputation site. However, if epinephrin is omitted, if the injection is made without excessive pressure, if the level of the block is a considerable distance proximal to the amputation site and if it is not used in the presence of ascending infection, it would seem that no appreciable circulatory or other complication should result. Another possible disadvantage of surgical amputation prior to chemosurgical treatment is the fact that the fixative is used more sparingly and for a shorter period of time than if the entire amputation were done chemosurgically. The resultant decrease in the chemical inflammation may well have an adverse effect on the reactivity and healing qualities of the tissues at the amputation site. That this may actually be the case is indicated by the fact that when prior surgical amputation is practiced the final layer of fixed tissue takes several days longer to separate, and it does not do so as cleanly. Moreover, the granulation tissue is not as healthy and well vascularized as it is after chemosurgical amputation without prior surgical removal. Whether this relatively sluggish reaction may reduce the incidence of ultimate healing of the amputation wounds requires further evaluation.

With the information now at hand it would seem that in patients in whom the circulation and reactivity of the tissues are of borderline character the safest procedure is chemosurgical amputation without preliminary surgical procedures. In patients with relatively good circulation and good reactivity, surgical amputation prior to the institution of chemosurgery is justifiable.

When preliminary surgical amputation is practiced it is carried out at a level approximately 1 cm. distal to the anticipated final level of amputation. Dichloracetic acid is used for hemostasis and for preliminary penetration of the stratum corneum; then zinc chloride fixative is applied. The thickness of the application of the fixative is less than half that used when the entire amputation is done chemosurgically. In patients with very poor circulation the amount of fixative must be reduced further still. The rest of the chemosurgical amputation is carried out in one or more stages in the same manner as if there had been no preliminary surgical amputation (Figs. 201 and 211).

The above-described methods are applicable to all forms of gangrene regardless of their cause. However, since there are a number of special considerations which require elaboration, each type of gangrene is considered individually.

Diabetic Gangrene

In diabetic patients there may be three abnormal conditions that tend to favor the development of gangrene: (1) the diabetic arteriosclerosis which results in circulatory impairment, (2) the diabetic neuritis which results in anesthesia which in turn predisposes to injury from nails in the shoes, hot water bottles, abnormal pressure and other forms of trauma, and (3) the reduced resistance to infection which allows ready entrance of organisms through minor abrasions, ingrown toenails, dermatophytosis or macerated corns or calluses.

In diabetic patients gangrene at times may develop largely as a result of the anesthesia and lowered resistance to infection even though the circulation is only slightly impaired. In such cases the relatively good circulation may result in prompt healing regardless of whether the gangrenous part is removed surgically or chemosurgically. However, with greater degrees of circulatory impairment surgical removal becomes progressively more likely to lead to the formation of small foci of necrosis whether these originate from sutures, ligatures or merely from the incisions themselves. These small foci readily become infected and gangrene may again develop and spread. Therefore, when there is doubt regarding the circulatory effi-

ciency the chemosurgical technic is preferable because no sutures or ligatures are used, no tension can develop in a flap of tissue no fluid can collect and no organisms can enter the accurately predict whether the circulation and reactivity of the tissues at a given level is sufficient to lead to healing following conservative amputation *Therefore, except in certain*



Fig 198. (A) Diabetic gangrene with exposure of interphalangeal joint and destruction of the distal phalanx. (B) *Granulation tissue ten days later* (C) Healed lesion.



Fig 199 (A) Diabetic gangrene of the second and fourth toes. (B) Healed lesion after chemosurgical amputation. The third and fifth toes though not frankly gangrenous, were removed because of the infected sinuses at their bases.

lesion until the final layer of fixed tissue is ready to separate by *which time the* wound is protected by the infection resistant granulation tissue Unfortunately *there is no way to* selected cases, the chemosurgical method of removal is preferable because it provides a greater margin of safety

Although superficial areas of necrosis affect

ing the toes occasionally may be removed without amputation of the digit it is customary to chemosurgically remove the toe to its base whenever the gangrene extends to the bone (Fig 196) or involves a joint (Fig. 198) During the amputation of a toe care is used to avoid entrance into the metatarsophalangeal joint unless a more proximal amputation is contemplated When the adjacent toes exhibit abnormalities such as hammer toe or when the gangrene extends too close to their bases it is involved, a transmetatarsal chemosurgical amputation results in a functional stump (Fig. 202)

In diabetic patients, osteomyelitis affecting a phalangeal or metatarsal bone is a chronic destructive process that usually eventuates in frank gangrene. Hence the affected tissue should be removed along with the portion of the toe distal to the lesion (Fig 203) The proximal extent of the process is readily discerned by gross visualization because the

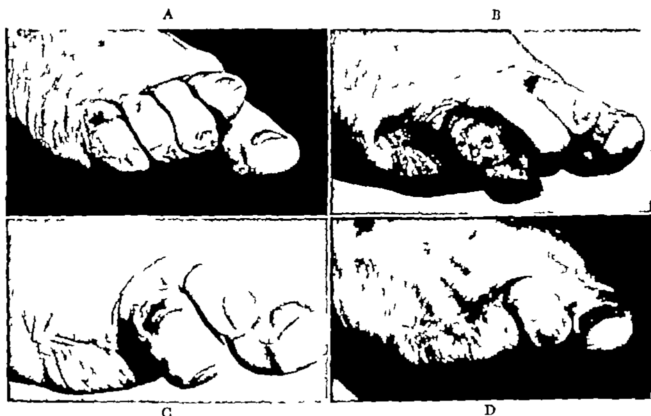


Fig. 200. (A–C) Diabetic gangrene affecting three toes successively at yearly intervals over a period of three years. (D) Healed lesion five years after the first amputation. The patient was ambulatory throughout.

advisable to remove them even though they are not yet gangrenous (Fig 199) Sometimes several toes become gangrenous one at a time over a period of years, but the patient can be kept ambulatory by simply removing the toes as they break down (Fig 200)

Gangrene which affects one or two metatarsal heads may necessitate amputation through the distal third of the metatarsals but, if possible, the toes less extensively involved should be amputated more conservatively in order to preserve a more useful foot (Fig 201) However even when all of the metatarsal heads are affected bone is soft and fragmented as contrasted with the hard normal bone.

Areas of gangrene or penetrating ulcers on the plantar surface usually arise under the metatarsal heads. If superficial they may respond to very conservative chemosurgical removal and enough of the plantar fat pad may be preserved to provide a stable scar However if the lesion is a penetrating ulcer which extends to a metatarsophalangeal joint, chemosurgical amputation of the toe through the distal third of the metatarsal is advisable (Fig. 204)



Fig 201 (A) Diabetic gangrene of all the toes and the first and fifth metatarsophalangeal joints. (B) Granulation tissue after amputation of all of the toes and of the heads of the first and fifth metatarsals. The major portion of the amputation was done surgically under local anesthesia and the last several millimeters were removed chemosurgically (C) Healed foot four months after amputation. The patient did not step on the foot until epithelization was complete in order to avoid the development of an overhanging plantar edge. With contraction of the scar the plantar pad pulled dorsalward protecting the ends of the bones on walking The patient was still walking on the foot after more than a year

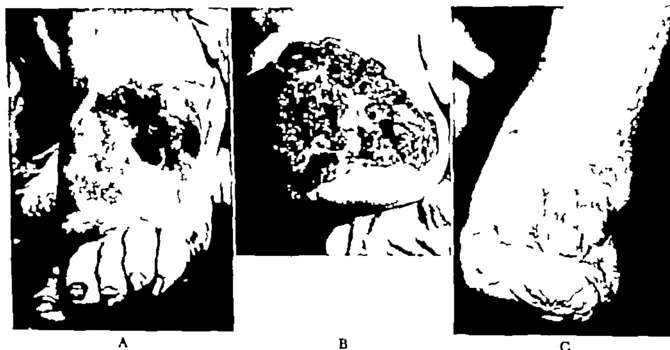


Fig 202. (A) Diabetic gangrene of the great toe and dorsum of the foot. There were many pus-filled, gangrenous sinuses honeycombing the anterior part of the foot. (B) Granulation tissue after chemosurgical amputation through the middle of the metatarsals. If sulfonamides or antibiotics had been available a more conservative amputation may have been feasible (C) Healed stump 10 months later Five years later the patient still was walking around on the stump without difficulty

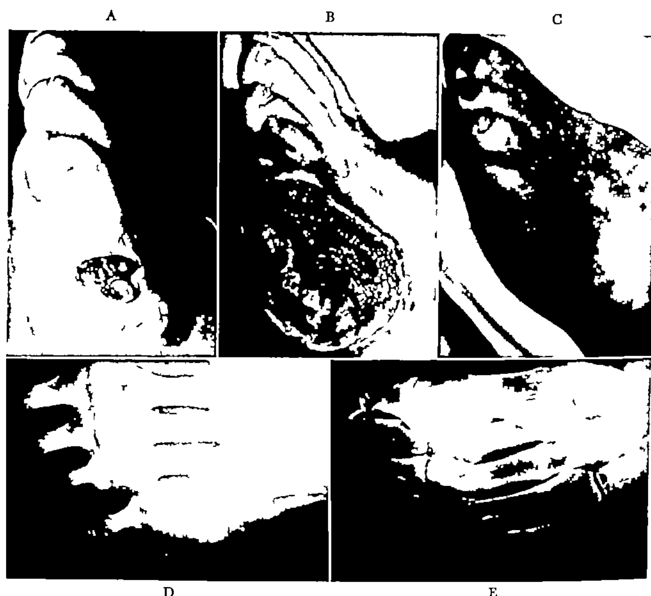
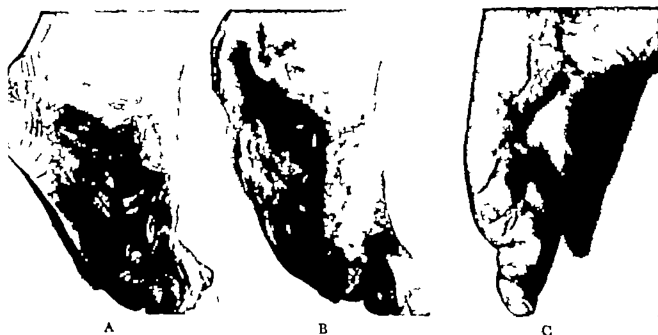


Fig 203 (A) Diabetic gangrene with draining sinus leading to fragmented bone. (B) Granulation tissue after chemosurgical amputation. (C) Healed lesion. (D) Roentgenogram showing destruction of bone around the metatarsophalangeal joint. (E) Appearance of bone after chemosurgical amputation.



A B C

Fig 204 (A) Penetrating ulcer with beginning destruction of the metatarsal head as revealed by x ray (B) Granulation tissue after chemosurgical amputation. (C) Healed lesion.



A B C

Fig. 205 (A) Diabetic gangrene of dorsum of foot and of the third toe. (B) Granulation tissue after removal of the gangrenous area and the third and fifth toes. The circulation of the fifth toe was interfered with and it was removed though not initially gangrenous. (C) Healed lesion.

Gangrenous areas on the dorsum of the foot also may be chemosurgically excised but if in the process the blood supply of an adjacent toe is impaired it also should be removed (Fig 205)

Gangrene as far proximal as the heel often indicates a poor prognosis as far as local treatment is concerned, but if it is not too extensive it may be successfully removed chemosurgically (Fig 206) If the gangrene affects the calcaneus, the involved bone also is removed but in such cases the prognosis for healing often is poor



Fig 206 (A) Diabetic gangrene of the heel. (B) Granulation tissue after chemosurgical excision. (C) Healed lesion.

Diabetic gangrene affects the fingers only rarely The conservative amputations made feasible by the chemosurgical method allows preservation of the greatest possible amount of function (Fig 207)

Arteriosclerotic Gangrene

This type of gangrene is much the same as diabetic gangrene both in its clinical features and in its response to chemosurgical treatment. However there are some differences. As compared with diabetic gangrene there is a greater tendency for circulatory deficiency to predominate over both nerve disturbances and susceptibility to infection as a causative factor This in turn tends to place more of the patients with arteriosclerotic gangrene in the group of cases in which the reactivity of the tissues is insufficient to throw off the final layer of chemically cauterized tissue.

The initial application of the fixative chemical may cause more pain in the patients with arteriosclerotic gangrene than in those with diabetic gangrene However the relief of pain within a few hours after institution of chemosurgical treatment is correspondingly gratifying Typically the patient with arteriosclerotic gangrene gets his first good night's sleep in weeks or months.

Often it is remarkable how a gangrenous toe that has exhibited no tendency to separate spontaneously for many weeks will clean up within two weeks after chemosurgical removal of the gangrenous tissue along with a few millimeters of normal tissue (Fig 208)

Frostbite Gangrene

Because the circulation usually is relatively good in patients with frostbite gangrene, the lesions heal regularly following chemosurgical amputation (Fig 209) The essential lack of circulatory impairment also makes it safe to amputate at a very conservative level. This results in the preservation of the greatest possible amount of tissue and function. It is ad

visable to wait one to three weeks after freezing in order to determine the exact amount of necrosis because if only a thin superficial layer is damaged it is not necessary to remove the entire toe.

frostbite or the burn yet after the chemosurgical removal of the gangrenous tissue along with a few millimeters of adjacent uninvolved tissue the fixed tissue separates in a week or so Apparently the reactivity of the tissues just

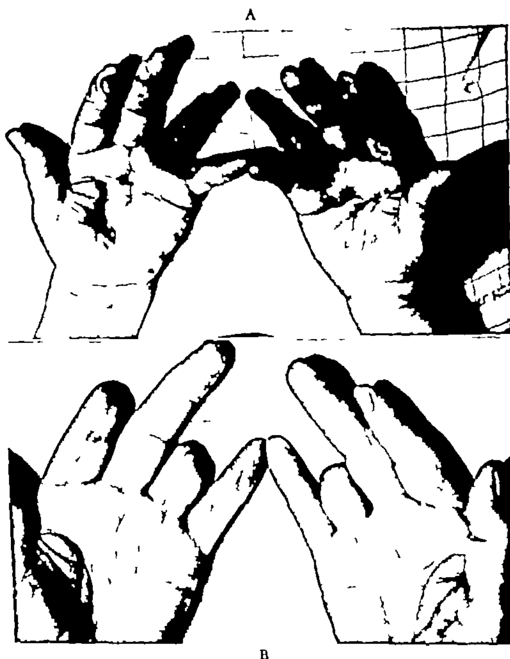


Fig 207 (A) Diabetic gangrene of the index and fourth fingers of both hands. (B) Healed lesions.

Tissue which has become gangrenous as a result of cold, in common with that which has become gangrenous as a result of thermal burns, tends to separate much more slowly than tissue that has been fixed with zinc chloride. Thus, there may be little tendency for the gangrenous slough to separate three or four weeks after the beyond the farthest extent of the gangrene is somewhat impaired by the freezing or burning but it is not affected adversely by the zinc chloride.

The chemosurgical technic also is useful in the conservative removal of frostbite gangrene of other areas. For example, the exposure of

the cartilage of the helix of the ear which may be the painful result of freezing may be corrected by the conservative chemosurgical removal of the damaged tissue.

The safety with which conservative amputation may be carried out even in the presence of gross infection suggests the practicality of its use in frostbite gangrene in military personnel. The technic also should be useful in trench foot or immersion foot, but as yet it has not been tried for these conditions.

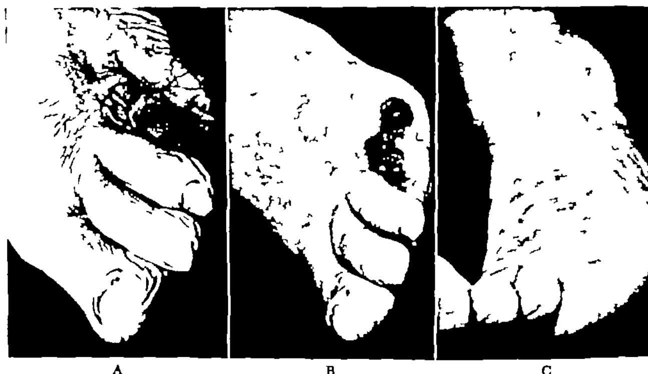
Thrombo-angiitis Obliterans with Gangrene

In gangrene associated with thrombo-angiitis obliterans or Buerger's disease the conditions for healing following chemosurgical amputation often are not favorable. In several cases the fixed tissue failed to separate and there was extension of the gangrene. In one case it was possible to clean up the wound after chemosurgical amputation but granulation tissue failed to form, epithelization did not take place and the persistent pain in the wound necessitated higher amputation.

However in selected cases in which the circulatory impairment is not too severe, conservative chemosurgical amputation may be carried out with success (Fig. 210)

Arterial Embolism with Gangrene

Occasionally gangrene forms as a result of the sudden occlusion of an artery by an embolus which usually originates from a vegetation in a rheumatic heart. The chemosurgical technic allows amputation to be carried out at a comparatively conservative level. This is especially desirable because when sufficient time has elapsed for the development of collateral pathways the circulation of the part may prove quite adequate.



A B C

Fig 208 (A) Senile arteriosclerotic gangrene of the fourth toe. The slough had remained adherent after three months of warm compresses at another hospital. (B) Granulation tissue twenty four days later The fifth toe also was chemosurgically amputated since its blood supply could not be preserved. (C) *Healed lesion.*

Arterial Thrombosis with Gangrene

Although thrombosis not infrequently is observed in patients with diabetic or arteriosclerotic gangrene this condition only occasionally arises independently and constitutes the primary cause of the gangrene. The chemosurgical amputation of the gangrenous part may be successful at a more conservative level than otherwise possible and when the collateral

pathways have become established the extremity may return to a fairly normal condition.

Raynaud's Disease with Gangrene

The vasomotor disturbances which characterize Raynaud's disease lead to trophic changes that occasionally may eventuate in and drugs infection including gas gangrene and injuries to vessels In some of such cases the chemosurgical removal of the gangrenous tissue may be advantageous. Thus one patient who was referred for removal of a poorly circumscribed gangrenous slough which formed in the cubital fossa as a result of a subcutaneous injection of glucose solution responded well to



Fig 209 (A) Frostbite gangrene following freezing of the feet three weeks before. (B) Granulation tissue after chemosurgical amputation of the toes. The heads of the metatarsals were removed from the right foot but not from the left. (C) Healed lesions. The lesion on the left foot was covered with a graft by Dr K. E. Lemmer while that on the right was allowed to heal by second intention. Though the grafted wound healed sooner it was not ready to support the weight any sooner

gangrene The chemosurgical amputation of the gangrenous portions of the digits may be carried out safely at a conservative level and upon removal of the painful lesion the circulatory status may improve (Fig 211)

Other Forms of Gangrene

Gangrene may develop on the extremities from other causes such as trauma chemicals chemosurgical removal of the damaged tissue. Toes which have become gangrenous as a result of trauma or infection also have been conservatively amputated by the chemosurgical technic with successful results. In several cases gangrenous sloughs in varicose ulcers of arteriosclerotic individuals were chemosurgically excised with improvement of the conditions for healing

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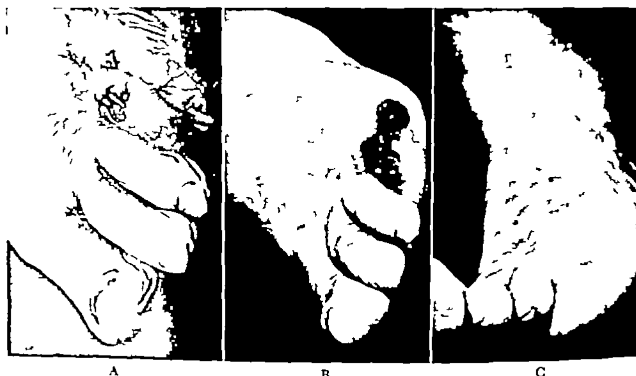


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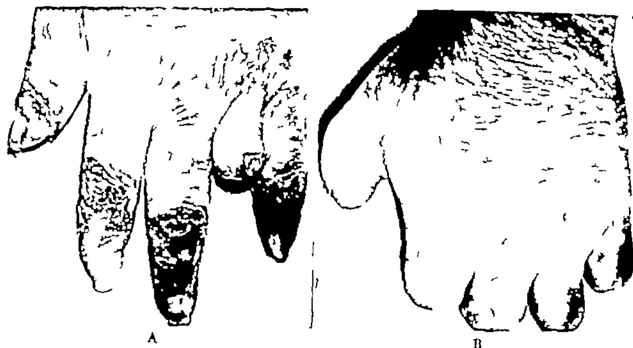


Fig 210 (A) Thrombo-angiitis obliterans with gangrene. The patient had lost several toes previously He resumed smoking, which had been forbidden, with this result. (B) Healed lesions. The left hand was similarly involved. The stumps of the fingers were useful in his work as a masseur

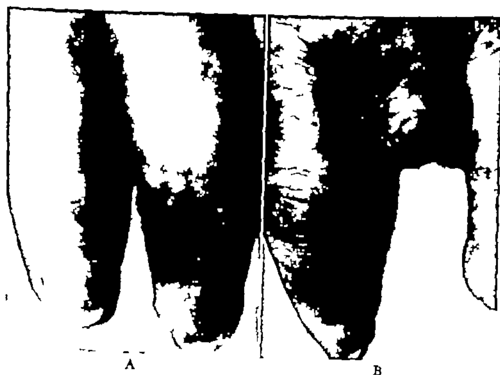


Fig 211 (A) Raynaud's disease with gangrene. (B) Healed lesion after amputation. The main portion was removed surgically under local anesthesia and the last few millimeters were removed chemosurgically

Results of Chemosurgical Amputation of Gangrenous Parts of Extremities

In the entire series of 248 patients there were 276 extremities affected by gangrene. Of the total number of lesions there was healing after chemosurgical amputation in 197. Therefore the rate of healing was 72.1 per cent for the entire group (Table XLVIII).

The results in diabetic gangrene were slightly better than in senile arteriosclerotic gangrene (72.8 *cf* 64.6 per cent). The poorer results in arteriosclerotic gangrene reflect the preponderant influence of ischemia as compared to diabetic gangrene in which infection and nerve

TABLE XLVIII
RESULTS OF CONSERVATIVE CHEMOSURGICAL AMPUTATION IN GANGRENE OF VARIOUS ETIOLOGIC TYPES

Etiology of Gangrene	*Number of Patients*	*Number of Lesions*	*Lesions Healed Number*	*Per cent*
Diabetic arteriosclerosis	166	188	137	72.8
Senile arteriosclerosis	62	64	41	64.6
Frostbite	8	11	11	100.0
Thrombo-angiitis obliterans	6	7	3	42.9
Arterial embolism	3	3	2	66.7
Arterial thrombosis	2	2	2	100.0
Raynaud's disease	1	1	1	100.0
Total, all types	248	276	197	72.1

disturbances also play a significant role. The rate of 100 per cent healing in frostbite gangrene is to be expected in view of the essential lack of circulatory impairment in most cases. The relatively low rate of 37.5 per cent in thrombo-angiitis obliterans appears to be due not only to severe circulatory deficiency but also to a peculiar lack of reactivity of the tissues in this disease. The numbers of cases of gangrene from embolism, thrombosis and Raynaud's disease were too small to provide significant statistical data but the good results which were obtained were not unexpected in view of the nature of these conditions.

The causes of the unsuccessful results which occurred in fifty-one patients with diabetic gangrene were as follows: failure of separation of the final layer of fixed tissue in twenty four, extension of the gangrene in thirteen, extension of infection in six, extension of gas gangrene in one, discharge before completion of treatment in one, and death from intercurrent disease in six. The causes of the unsuccessful results in twenty three patients with arteriosclerotic gangrene were as follows: failure of separation in six, extension of gangrene in seven, discharge before completion of treatment in two and death from intercurrent disease in eight.

It may be that preliminary surgical removal of most of the involved tissue before the institution of chemosurgical treatment may affect the results. In the series of thirteen cases in which this procedure was carried out there were eight patients in whom healing progressed satisfactorily (eg., Figs. 201 and 211). In five cases the final layer of fixed tissue failed to separate. Thus healing occurred in 61.5 per cent of the patients, a rate somewhat below the 72.1 per cent obtained by the use of the chemosurgical technic alone. However, a series of thirteen cases is far too small to permit definite conclusions.

Prediction of Outcome

In order to determine what factors are most important in predicting the outcome of chemosurgical amputation, almost all referred cases were accepted for chemosurgery whether or not it was thought that the circulation was adequate to permit healing. From the data so obtained the following significant prognostic criteria evolved:

(1) Diabetic gangrene has a better prognosis than arteriosclerotic gangrene owing largely to the predominance of infection and neuropathy in the causation of many cases of diabetic gangrene as contrasted to the predominant influence of ischemia in most cases of arteriosclerotic gangrene.

(2) The younger the patient the better the prognosis.

(3) The more definite the line of demarcation between the gangrenous tissue and the living tissue the better the prognosis.

(4) The greater the reaction of the living tissue to the gangrenous tissue as indicated by redness, swelling, heat and inflammatory exudate the better the outlook. In other words,

a wet gangrene in an inflamed foot usually signifies a better prognosis than a dry ischemic gangrene in a pale cool, unswollen foot.

(5) In general strong pulsations in the *dorsalis pedis and posterior tibial arteries* are good prognostic signs, but their absence does not necessarily indicate a poor prognosis because collateral circulation may be adequate.

(6) A high degree of arteriosclerosis as indicated by a palpable thickening of the radial vessels and by calcification as shown in roentgenograms of the feet is often indicative of a poor prognosis but not necessarily so because a good arteriolar and capillary circulation may be present in spite of markedly sclerotic arteries. An investigation is currently under way to determine whether microscopic appraisal of the degree of involvement of the smaller vessels may be of value in determining the outlook for healing at a given level.

(7) The histamine wheal test is an excellent indicator of capillary function and hence, of prognosis, but the same information usually can be obtained by observation of the degree of inflammatory reaction to the gangrene. Therefore the wheal test is no longer used routinely

Without appreciable prognostic value were the following factors the rapidity with which the gangrene progressed the extent of the gangrene unless the major part of the foot were involved, and the presence of bone destruction. In diabetics, the duration, severity and control of the diabetes were relatively unimportant in estimating prognosis

In a *study which was reported* in collaboration with Drs. E. L. Severinghaus and E. R. Schmidt[14] it was found that the efficiency of the circulation in the extremity was a prime *factor in determining the outcome after con*servative chemosurgical amputation. This was indicated by the finding that in extremities in which the circulation was rated as "fairly good," healing resulted in 93.8 per cent of the cases while in extremities in which the circulation was rated as "fair" or "poor" healing resulted in 29 4 per cent of the cases. However the fact that 29 4 per cent successful results were obtained in extremities with only poor or fair circulation indicates that either the available prognostic criteria are not infallible or *there is something besides the efficiency of the* circulation that affects healing at the amputation site. Apparently the reactivity of the living tissues as indicated by their ability to *throw off the fixed tissue*, is not always closely proportional to the efficiency of the blood supply

The therapeutic test provides the only certain means to determine whether a conservative chemosurgical amputation will lead to healing If after ten days the separation of the final layer of fixed tissue is progressing well the outlook for healing is good. However if the fixed tissue is still firmly adherent the prospects of healing at the conservative level are remote.

Discussion

Why would not surgical amputation be as successful as chemosurgical amputation if carried out at the same level in a similar group of patients? There are three main reasons. (1) The field usually is more or less infected and the fresh-cut surfaces with their open tissue spaces are more susceptible to the spread of infection than are the infection resistant granulations following chemosurgical amputation. Moreover the area is sterilized during chemosurgical treatment by the fixative chemical. (2) Following surgical amputation there are minute areas of necrosis not only from the sutures and ligatures but also from the incision itself Under adverse conditions these necrotic foci may lead to the formation of collections of fluid which may, in turn, lead to abscess formation and further extension of the gangrene Following chemosurgical amputation there are no such areas of necrosis in the tissues adjacent to the final layer of fixed tissue. (3) *Gangrenous sinuses* which may extend for unexpected distances along tendon sheaths, fascial planes or other structures cannot be located as accurately during surgical amputation *as they can during* chemosurgical amputation. Therefore the chance of leaving a residuum of gangrenous tissue is greater after conservative surgical amputation than after chemosurgical amputation Of course the danger of cutting across a gangrenous sinus may be obviated by performing the surgical amputation at a much more proximal level, as

for example by doing a transmetatarsal amputation for gangrene involving a toe

Due to the lack of data concerning the results of surgical amputation at levels similar to those at which the chemosurgical amputations were made it is impossible to accurately compare the results of the two methods of amputation. However there are reports of the results obtained by surgical amputation at the transmetatarsal level

The first reported series of transmetatarsal amputations was begun by Furste and Herrmann in 1934 [14] No attempt was made to close the wounds. These authors obtained satisfactory healing in 37 per cent of the patients with diabetic gangrene and in 31 per cent of the patients with arteriosclerotic gangrene In 1944 when penicillin became available McKittrick,[11] Franseen[22] and their co-workers began a series of transmetatarsal amputations with immediate suture of the wounds. The results as reported by Root[19] indicate a successful outcome in 84.2 per cent of 122 cases of diabetic gangrene Although this rate exceeds the 72 8 per cent rate of healing following chemosurgical amputation, there were two differences between the two series that must be taken into account. First, the group of surgically treated patients included a larger proportion with the predominantly neuropathologic type of disease, as compared *to the predominantly circulatory* type, than was the case in the group of chemosurgically treated patients. In the latter series practically every patient with gangrene sufficiently limited to allow preservation of a useful foot was accepted for treatment regardless of whether the predominant causative factor was neuropathologic or circulatory As has been stated if the cases of the patients with 'poor' and "fair" circulation are omitted and only those with "fairly good" circulation are included, chemosurgical amputation results in healing in 93 8 per cent of the cases. The second difference between the two series was that the chemosurgical amputations in practically all cases were carried out at a more conservative level than were the surgical transmetatarsal amputations. This conservatism may have had a slightly adverse effect on the percentage of lesions healed, but it resulted in the preservation of the useful transverse plantar arch in a high proportion of the cases

Every effort to save as much of the foot as possible is worth while because the elderly patients with gangrene do not readily adjust to the loss of a portion of the extremity The chemosurgical technic makes it possible to successfully amputate a toe even if the gangrene has reached the web between the toes Surgical amputation under such circumstances is not often attempted and is still less often successful because there is not enough tissue to allow closure without tension Inasmuch as the gangrene approaches or reaches the base of the toe in a considerable proportion of the cases it is evident that many more will be amenable to conservative chemosurgical amputation than to equally conservative surgical amputation

While ambulation is easier when the transverse plantar arch has been preserved the stump following transmetatarsal amputation still is quite satisfactory and certainly it is much better than the loss of the limb A great many patients who have lost a leg because of gangrene never learn to use an artificial limb Therefore even though the extremity has a considerable degree of circulatory impairment and even though it may be subject to further gangrene it is justifiable to give the patient the use of the extremity for as many years as possible Inasmuch as the arteriosclerosis *usually involves* the vessels of the heart, brain kidneys and other vital organs, the life expectancy usually is not long hence the patient often can be kept ambulatory until he develops a fatal intercurrent illness.

The operative risk of chemosurgical amputation is low In the present series there were no deaths that were directly attributable to the procedure itself because no general anesthetic was used and there was nothing about the procedure that could cause shock or other complications. However the elderly diabetic and arteriosclerotic patients are subject to various degenerative diseases which can cause death during amputation or during the separation of the final layer of fixed tissue. In the present series of 248 patients there were nine deaths during this period. Thus the mortality rate may be considered to be 3 6 per cent even

though the deaths were not the result of the operative procedure itself. The mortality rate in the series of 166 cases of diabetic gangrene was 8 per cent. This rate is about the same as would be expected in a group of elderly arteriosclerotic diabetics within a similar period of time even if no operation were carried out. In the series of sixty two cases of arteriosclerotic gangrene the mortality rate was 6.5 per cent.

As has been stated, the conservative chemosurgical amputation of a gangrenous toe or other part of the foot does not adversely affect the outcome of subsequent amputation of the leg should this procedure prove necessary. Thus, in the entire series, amputation of the leg was necessary in fifty cases of these five died of the operation or of postoperative complications, a mortality rate of 10 per cent. This is a low figure, especially in consideration of the fact that these were the patients in whom the circulation was so poor that conservative chemosurgical amputation was unsuccessful. For the series of thirty four diabetic patients who came to amputation of the limb by various members of the surgical staff after unsuccessful chemosurgical treatment the mortality rate was 11.8 per cent. For the series of eleven arteriosclerotic patients who came to amputation the rate was 9.1 per cent.

Following chemosurgical amputation of a gangrenous toe or other part of the foot, it is not unusual to observe a definite improvement in the circulation in the remaining tissues. Although some of this improvement may be the result of the reduction of the demands upon the limited available blood supply and some may be the result of the development of a collateral circulation, part of it often appears to be due to a decrease in vasospasm. Whether the reduction of the vasospasm is the result of of the removal of the gangrenous lesion which acts as the beginning of a reflex arc or whether it is the result of other factors is not certainly known. Regardless of the cause of the improved circulatory status after chemosurgical removal of a gangrenous part, the fact that it sometimes is observed is one of the reasons why many patients have been accepted for conservative chemosurgical treatment in spite of very poor circulation in the extremity.

Some patients and their physicians are inclined to wait for spontaneous sloughing of gangrenous toes or other parts. While this may be justifiable for very superficial gangrenous lesions it is not recommended for deeper lesions because the process is very time-consuming and usually unsuccessful. Chemosurgical amputation not only gives a much better chance of healing but it saves much time because under favorable conditions the final layer of fixed tissue separates in ten days. When separation fails to occur in that time it may be concluded that no conservative procedure would have any chance of success certainly spontaneous separation of the gangrenous slough could not have been expected in such cases.

Since sulfonamides and antibiotics have become available the results of chemosurgical treatment have improved. The first half of the present series was carried out without benefit of these drugs. The control of infection during that period required wide incisions of infected tracts and, in some cases, chemosurgical tunnelling procedures for the purpose of cleaning out infected tracts without the loss of the overlying tissue.[44] Such procedures now are rarely needed since infections usually can be kept under control by systemic therapy with antibiotics or sulfonamides. The result is less mutilation and fewer cases which are unsuccessful because of ascending infections.

The chemosurgical removal of gangrenous flaps which may occur after surgical amputations has been successfully carried out in several cases. It is suggested that this technic might be particularly useful in the treatment of the gangrene which occasionally develops in the dorsal flap following transmetatarsal amputations.

CHAPTER 29

Other Gangrenous Conditions

ALTHOUGH much less common than gangrene of the extremities gangrene of the skin and subcutaneous tissues of other parts of the body occasionally occurs The chemosurgical treatment of such gangrenous lesions not only permits the accurate and conservative removal of the necrotic tissue but it also eliminates part or all of the infection which almost invariably accompanys the condition.

The chemosurgical technic is essentially the same as that outlined for gangrene of the extremities. In some cases the fixative is applied to the gangrenous area before any tissue is excised. In other cases it is more expedient to surgically excise the main mass of necrotic tissue under local anesthesia prior to the application of the fixative chemical. Of course simple debridement, with or without local anesthesia often is all that is needed especially if the gangrenous tissue is about ready to slough spontaneously However not infrequently there are conditions such as ischemia infection or scarring that retard or prevent separation of the necrotic tissue. In such cases the chemosurgical excision can be carried to a level at which the tissues are fully viable with consequent rapid separation of the final layer of fixed tissue and prompt epithelization.

Gangrene may result from a variety of causative factors such as infections, chemical agents, pressure, and ischemia from trauma or from neurotrophic disturbances. Only a few of the more common types of gangrene need be mentioned here

Decubitus Ulcers

The necrotic tissue which may result from pressure over bony prominences in bed ridden patients may be removed chemosurgically The resultant clean granulating surface provides improved conditions for epithelization or for grafting Needless to say the pressure and inanition that led to the bed sore should be corrected as much as possible in order to prevent recurrence When the gangrenous process extends into the underlying bone the osseous tissue may be fixed with the zinc chloride fixative and then removed with a chisel or rongeur until a level is reached at which the bone is healthy enough to support epithelization. After separation of the final layer of fixed tissue the wound may be dressed with scarlet red gauze which promotes the growth of the epithelium and provides an antiseptic effect.

Trophic Ulcers

The necrosis which may result from neurotrophic disturbances in patients with such neurologic diseases as transverse myelitis or syringomyelia may produce particularly intractable ulceration. The chemosurgical removal of the necrotic and devitalized tissue may be helpful in cleaning up the wound but the persistent trophic disturbance is likely to prevent complete epithelization. However the condition of the lesion may be improved to such an extent that surgical closure or grafting becomes feasible.

Gangrene of the Skin

This condition which also goes by the names of dermatitis gangrenosa pyoderma gangrenosum and sphaceloderma is an entity of diverse etiology It may arise in pyogenic infections such as carbuncles, in erysipelas, in gas gangrene in severe exanthematous diseases, in association with chronic granulomas such as lupus vulgaris, gumma or leprosy and in trauma especially if

large vessels are involved. Often there is an undermined necrotizing border which advances into the ischemic tissues at the periphery. The chemosurgical removal of the gangrenous tissue plus a border of the devitalized tissue at the periphery usually stops the necrotizing process. The fixative destroys the infective organisms including the anaerobic streptococci, staphyococci and diphtheroids which may be harbored under the overhanging edges. With the control of the infection the metabolic needs of the tissues are reduced and the tendency of the gangrene to spread is eliminated.

Burn Sloughs

The chemosurgical removal of the tissue which has become necrotic as a result of burns along with a few millimeters of the adjacent viable tissue results in separation of the slough in approximately one week instead of the two or three weeks which is usual if it is allowed to separate spontaneously. As a result the wounds heal more rapidly and the scars are soft, smooth and pliable as contrasted with the thick, hard, rough scars that often follow burns. In several arteriosclerotic and diabetic patients burn sloughs from heat lamps and hot water bottles were removed in this manner with rapid and uncomplicated healing. The use of the chemosurgical method for the removal of necrotizing lesions from overexposure to radium or roentgen rays is described in the chapter on precancerous lesions.

PART IV

INFECTIONS

CHAPTER 30

Infectious Granulomas

CERTAIN types of infected lesions are amenable to chemosurgical treatment. Some of these such as warts molluscum contagiosum and granuloma pyogenicum were discussed under the heading of tumors of infectious origin (Chapter 26) while chronic infected ulcers and radiation ulcers were discussed under the heading of precancerous lesions (Chapter 27) With the advent of sulfonamides, antibiotics and other systemic medicaments an ever increasing number of infections may be brought under control without local treatment. However certain infections which retain some degree of refractoriness to systemic treatment may be treated advantageously with chemosurgical technics. Among the diseases of this nature are some of the chronic infectious granulomas, notably lupus vulgaris and blastomycosis.

Lupus Vulgaris

The precancerous potentialities of this disease have been described and illustrated in the chapter on precancerous lesions (Fig 195) Lupus vulgaris is caused by the tubercle bacillus and is characterized initially by macular or papular infiltrations made up of granulomatous tissue which upon diascopy exhibit a brownish red, "apple jelly" color Variable amounts of ulceration, scar and hyperkeratosis are present in chronic lesions. The face is the most common site but the extremities and other parts of the body may be affected Microscopically the typical tubercles are composed of central giant cells surrounded by epithelioid cells and a peripheral zone of lymphocytes and plasma cells while the overlying epithelium often becomes acanthotic and hyperkeratotic.

Lupus vulgaris lesions which persist for long periods despite appropriate systemic treatment and general hygienic measures should be removed in order to prevent cancerous change. Since lupus vulgaris has a characteristic histopathology the microscopic control provided by the chemosurgical method serves to indicate exactly how much tissue to remove. The zinc chloride kills the tubercle bacilli and unless the organisms have infiltrated into the tissues beyond the level of removal no recurrence is likely to take place As a consequence of the conservative level of removal the cosmetic results are satisfactory (Fig 212) Other forms of tuberculosis on the exterior of the body which may be amenable to chemosurgical treatment are discussed in Chapter 32

Nine patients with one or more lupus vulgaris lesions were chemosurgically treated. No recurrence was noted in six patients observed for periods of three months to eight years. One patient did not return for check up after treatment One patient reported recurrence after the lesions had remained healed for nearly two years subsequent treatment elsewhere with ultraviolet light was stated to have controlled the disease

Blastomycosis

This is the most common infectious granuloma of the skin in midwestern United States. The blastomyces which are yeast like organisms, usually enter the skin through small abrasions. The initial lesion is a papule which soon becomes a pustule This spreads to form a placque which is elevated several millimeters above the skin surface After variable intervals the uncontrolled disease may spread to the lungs and elsewhere causing death in some cases. Characteristic features of the cutaneous



Fig. 212 (A) Lupus vulgaris of eight years duration in a fifteen year old boy The patient had been in a tuberculous sanitorium for seven months and had received ultraviolet and roentgen therapy without improvement of the lesion. (B) Healed lesion six weeks after chemosurgical excision. There was no recurrence after eight years.

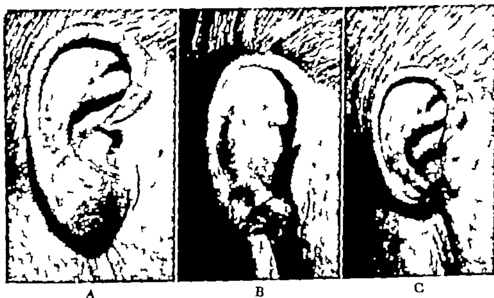


Fig 213 (A) Blastomycosis. (B) Granulation tissue and cartilage after chemosurgical removal. The diseased tissue extended unusually deep into the lobe. (C) Healed lesion One month later another lesion was chemosurgically removed from a finger There was no recurrence after three years.

patches are the steeply inclined margins, the papillation of the surface, and the small intra epidermal abscesses which may open and form crusts (Fig 213) Microscopically the characteristic small doubly refractile blastomyces usually can be observed in the intraepidermal abscesses. This feature plus the leukocytic infiltration, hyperkeratosis and pseudoepitheliomatous hyperplasia forms a characteristic microscopic picture which makes it feasible to

follow the progress of excision microscopically by means of the chemosurgical technic

Cutaneous lesions which do not respond promptly to systemic therapy should not be allowed to persist lest the disease spread internally. They may be removed rapidly and completely by means of the chemosurgical technic (Fig 213) While all of the lesions in the present series were removed by means of chemosurgical excisions alone, preliminary surgical excision under local anesthesia followed by chemosurgical excision should give just as good results. The microscopic control may be attained in the same manner as in the treatment of cancer and it should be used whenever there is any doubt as to the extent of the lesions. However gross visualization in some cases is sufficiently accurate to assure complete removal.

The results in a consecutive series of seventeen blastomycotic lesions which occurred in fourteen patients were almost uniformly successful. In only one patient was there known to be a recurrence this was a lesion on the tip of the nose which recurred at the periphery of the scar and which was subsequently eradicated by means of roentgen therapy and potassium iodide. This case was one of the first of the series and in retrospect was known to have been treated inadequately In another similar case there was a successful outcome (Fig 214)



Fig 214 (A) Blastomycosis (B) Granulation tissue after chemosurgical excision of the relatively superficial lesion. (C) Healed lesion. There was no recurrence after sixteen months. A large lesion which was removed from the leg also did not recur

The number of blastomycotic lesions on the various areas of the skin were as follows five on the nose four on the lower extremities two on the upper extremities two on the lower eye lid and one each on the trunk, neck, ear scalp and cheek. All of the lesions were allowed to heal spontaneously after chemosurgical excision except two which were covered with grafts because of their large size One large lesion at the base of the neck was one which had recurred after roentgen therapy in doses sufficient to cause a deep radiation ulcer the chemosurgical excision of both the blastomycotic and the radiation lesions resulted in permanent healing One large lesion on the thigh was eradicated after the lesion had continued to spread despite numerous roentgen treatments, electrosurgical excision, ultraviolet rays, silver nitrate cauterization and various ointments. Since blastomycosis usually is fairly superficial the scars often are quite good (Fig 215) As far as could be determined none of the patients in this series developed blastomycosis in the lungs or other internal organs.



Fig 215 (A) Blastomycosis. (B) Granulation tissue after chemosurgical excision of the superficial lesion. (C) Healed lesion. There was no recurrence after one year

Actinomycosis and Other Infectious Granulomas

One patient with actinomycosis affecting the submaxillary region was treated chemosurgically. The granulomatous lesion may have the clinical appearance of a carcinoma or sarcoma but when it breaks down the discharged pus contains the Streptothrix actinomyces or ray fungus organisms which form yellow granules of pinhead size. Histologically the granulation tissue usually is composed of tubercles with *epithelioid cells, giant cells, lymphocytes* and the pathogenic organisms. In order to prevent spread of the disease to other parts of the body where its presence may cause serious illness or death, the lesions should be removed promptly if systemic therapy has been unsuccessful.

Other infectious granulomas may have cutaneous lesions which occasionally might constitute indications for chemosurgical treatment. Among these may be mentioned certain phases of syphilis, yaws, pinta granuloma inguinale, lepra coccidioidomycosis, brucellosis, tularemia, histoplasmosis and sporotrichosis. Non-infectious granulomas which might be chemosurgically excised are beryllium granuloma, eosinophilic granuloma, foreign body granulomas and granuloma annulare. Except for one successfully treated patient with the last named type, the author has had no experience with these conditions. However, from the favorable response of granuloma pyogenicum and some of the infectious granulomas, a good result might reasonably be expected.

CHAPTER 31

Pilonidal Sinuses and Other Infected Tracts

SINCE pilonidal sinuses and other tracts are almost certain to be infected when they come to the attention of a physician it is justifiable to place them in the section on infections It is recognized however that infection usually is not the primary initiating factor The chemosurgical technic is useful in the treatment of these conditions because it provides a reliable means for visualization and removal of the tracts.

Pilonidal Sinus

Pilonidal sinuses, and the cysts which form if there is no patent opening are developmental defects which usually are located in the sacral and coccygeal regions. The lesions usually become symptomatic in young adulthood when infection sets in as a result of trauma or unusual irritation such as may be produced by long rides in a car The disease is so common in military personnel that it has popularly become known as "jeep disease It was the great loss of time in the treatment of this disease in a local military hospital that suggested the possibility of using chemosurgical methods for the removal of pilonidal sinuses particularly those which were recurrent and complicated

In the eleven years preceding the present writing eleven patients with pilonidal sinus were treated chemosurgically Of this number eight had had one or more previously attempted excisions and most of the lesions were large and complicated. In spite of the unusually high proportion of recurrent complicated sinuses, every one of the eleven lesions is currently healed.

The technic used in the first eight cases was the chemosurgical method without prior surgical excision. In the last three cases the tracts first were excised surgically following which chemosurgical excisions were made to make sure no sinuses had been missed Regardless of which method is used the purpose is to unroof the sinuses and cysts and to follow out all of the tracts in the bloodless chemosurgical field

In order to save time and reduce the discomfort to the patient the visible sinuses and cysts now initially are surgically excised under local anesthesia. This may be done very conservatively because any remaining sinuses can be followed out later by means of the chemosurgical technic A saucerized wound is produced by the surgical excision and the capillary bleeding is stopped by cauterizing the surface with dichloracetic acid Larger bleeders are coagulated by means of zinc chloride fixative impregnated gauze squares held in place under momentary pressure

The locations and depths of any remaining sinuses can readily be seen or located by means of a probe The sinuses so located may be excised immediately or they may be cauterized with dichloracetic acid and zinc chloride so they may be excised several hours later The latter procedure usually is followed because the smaller sinuses may be more accurately located in the firm fixed tissues which result from fixation with zinc chloride. Moreover the zinc chloride tends to make the separation of the final layer of cauterized tissue more rapid and clean.

In the present series of cases in which most of the patients had had one or more unsuccessful surgical excisions there were found a great many irregular tracts. These followed no definite pattern although there were many in which there was unexpected extension in the direction

of the rectum either in the midline or near to it. An important point is the fact that in practically every case the tracts extended much farther than would be expected from the external appearance of the lesions. Although an epithelial lining could be demonstrated microscopically in some of the previously untreated sinuses, there were only occasional epithelial remnants in the lining of many of the old recurrent lesions. Apparently the pus-filled pockets often pushed out into the surrounding tissues where epithelium-lined tracts had never been. In some of the cystic spaces loculation and partial organization were observed and although these could be cleaned out readily and the radiating tracts located chemosurgically it was evident that localization by means of injected dye into such spaces could not have been relied on to accurately stain all of the smaller tracts so they could have been located during surgical excision. For the same reason the treatment of pilonidal sinuses by the injection of a sclerosing solution could not be expected to yield reliable results.

In cases in which there was acute inflammatory swelling it made little difference whether chemosurgical treatment was started immediately or whether subsidence of the infection under antibiotic therapy was awaited. However in the presence of surrounding cellulitis antibiotic or sulfonamide therapy should be instituted immediately

All of the sinuses are not necessarily connected to the main ones. Not infrequently other small sinuses usually in the midline, may be detected by the use of a small probe. If these sinuses are very shallow all that need be done is to cauterize the lining with dichloracetic acid and a small amount of zinc chloride fixative.

Upon completion of chemosurgical treatment the final layer of cauterized tissue is covered with petrolatum gauze. As the fixed tissue begins to loosen in three or four days there may be a little drainage and there may be some discomfort from traction on the nerves attached to the slough. By four or five days the nerves and fibrous strands can be snipped with sharp-pointed scissors allowing removal of the layer The resultant granulation tissue is quite resistant to infection but efforts should be made to keep the wound clean till healing is complete. In some cases scarlet red gauze is applied and the cavity filled with sterile cotton. In other cases mercurochrome is applied to the wound and a dry dressing is used to bridge across the defect. The latter may be preferable for the patient who is to have the dressing applied at home.

The lesions usually heal within a month with healthy pliable scars (Fig 216) As has been stated, all of the eleven patients in the present series are healed at this writing and some have been healed for ten years or longer All of the lesions healed promptly and permanently with two exceptions one had a very deep tract extending up the anterior wall of the sacral canal necessitating several cauterizations of this one remaining tract over a period of three years before healing was complete. The other case of delayed healing was in a patient with a very deep gluteal cleft in which perspiration collected causing a dermatitis which, in turn, resulted in a break down of small areas of epithelium on several occasions over a period of a year An additional factor in the latter case was the irritating effect of the stiff hairs of the buttocks these tended to penetrate the delicate skin in the base of the cleft. When the hairs were removed by electrolysis and the patient instructed to keep the cleft dry and clean, the lesion remained healed. Incidentally the hair in most of the pilonidal sinuses in this series were observed to consist of hairs shed from the adjacent buttocks rather than being formed in hair follicles in the sinus tract itself. In some individuals the hairs are directed toward the thin skin in the base of the gluteal cleft, and the possibility is suggested that some of the lesions arise as a result of these hairs penetrating the skin and lodging in the underlying tissues rather than as a result of a true developmental defect.

Other Infected Sinus Tracts

A number of infected tracts of other types were excised chemosurgically in essentially the same way as were the pilonidal sinuses. Examples which may be cited are the following (1) A bullet injury in the form of an infected tract through which infected cerebral tissue



Fig 216. (A) Pilonidal sinus with cyst formation. The lesion had recurred shortly after surgical excision four years before. (B) Granulation tissue after chemosurgical excision. (C) Healed lesion. There has been no recurrence after ten years.

had herniated was cleaned out chemosurgically so that the fragments of the bullet could more safely be removed. (2) An infected heavily scarred fistulous tract which resulted from the drainage of an empyema cavity was chemosurgically excised with elimination of the infection and removal of the necrotic slough which had impeded healing. (3) A chronically infected cystic tract near the nipple of the breast was conservatively removed and at the same time malignancy was ruled out by thorough microscopic examination. (4) A brucellosis infection in the form of a sinus tract extending to a prepatellar abscess was chemosurgically excised. The wound healed and the troublesome focus of infection was eliminated. (5) An infected post mastoidectomy tract was chemosurgically cleaned out and widened to improve drainage and allow healing.

The advantages of the chemosurgical method for the removal of these various infected sinus tracts are (1) the accuracy with which all of the ramifications of the sinuses can be followed out, (2) the completeness with which the area is sterilized by the fixative and (3) the excellent conditions for healing afforded by the healthy granulation tissues which result after fixation of tissues with zinc chloride.

CHAPTER 32

Miscellaneous Infections

A VARIETY of infections have been treated chemosurgically either for the purpose of ruling out neoplastic disease or in order to eliminate an infection that had failed to respond to therapy with antibiotics, sulfonamides or other drugs. The conditions described here with are those with which I have had experience but undoubtedly there are other types of infections which also might be amenable to chemosurgical treatment.

Hidradenitis Suppurativa, Acne Conglobata and Dissecting Cellulitis of Scalp and Neck

These conditions are considered together because they all tend to have the same manifestations, namely abscesses, communicating channels, discharging sinuses, double comedones, keloid formation and so-called bridge scars. Hidradenitis begins in the apocrine sweat glands and usually affects the axillae, perineum and nipples where the apocrine glands are most numerous. Acne vulgaris which initially affects the sebaceous glands may lead to acne keloids, acne conglobata and dissecting cellulitis of the scalp and neck. Not infrequently chemosurgical technics are useful in unroofing and cleaning out the infected sinus tracts which are the intractible features of these conditions.

If there is appreciable cellulitis which had *not been controllable by antibiotic therapy the* safest procedure is to apply dichloracetic acid and zinc chloride fixative in order to produce



A B

Fig 217 (A) Acne conglobata and dissecting cellulitis of the neck following severe acne contracted in the South Pacific. The patient had been hospitalized elsewhere for fourteen months. The lesions were not appreciably benefited by roentgen therapy penicillin locally and systemically sulfonamides, staphylococcus toxoid, autogenous vaccine, stilbesterol, boric acid compresses, and ointments containing sulfur chlorophyll, bacitracin and other medicaments. (B) Healed lesion three months after chemosurgical removal of the multiple infected tracts which contained pus, epithelial remnants and hairs.

fixation of the surface tissues preparatory to entering into and cleaning out the sinus tracts However, if there is not much cellulitis procaine is injected around the affected area and the tracts are unroofed surgically Regardless of which way the tracts are entered they then are curetted out and the lining is thoroughly cauterized with dichloracetic acid Care should be exercised to follow out all of the ramifications of the system of tracts. If there is appreciable scarring around the tracts the zinc chloride fixative may be applied not only for the purpose of removing the scar tissue but also for the purpose of producing the best possible commonly become confluent and form keloid like masses The initiating low grade infection is the source of the fibrous tissue proliferation and a granulomatous type of infiltration There may be some pustules and brush like collections of hairs in enlarged hair follicles Eventually there is some loss of hair because of the destruction of the hair follicles and because of the heavy scarring

The lesions may be chemosurgically excised without loss of the bottoms of the hair follicles except where the process is exceptionally deep Accordingly a minimal amount of hairless scar is formed (Fig 218C) In the absence of cellu



Fig. 218. (A) Dermatitis papillaris capillitii of four years duration (B) Granulation tissue after chemosurgical excision. The bottoms of most of the hair follicles were preserved. (C) Healed lesion. There was no recurrence after two years.

granulation tissue after the chemically cauterized tissue has separated. After removal of the diseased tissues the resultant saucerized wound is covered with double thickness petrolatum gauze and the cavity is packed with cotton. In a week or less the final layer of fixed tissue demarcates so it can be dissected off In some instances it may be possible to close the wounds with sutures and get a linear scar but if this is not feasible the wound is allowed to heal by second intention (Fig 217)

Dermatitis Papillaris Capillitii

This is a perifollicular inflammatory process which affects the nape of the neck (Fig 218A) It is characterized by multiple papules which litis the same result may be obtained by infiltrating with procaine excising a layer as thick as necessary to eliminate the process and cauterizing with dichloracetic acid If further penetration is desired zinc chloride fixative also may be applied

Non-specific Infections

A large number of infected lesions of non specific nature have been removed because they looked like possible neoplasms or because they did not respond to the usual treatments for infections Most of these lesions were the result of pyogenic infection, usually of staphylococcal or streptococcal origin. Some produced persistent ulcers, others developed under the skin

lymphocytes. Thus, when there is doubt as to the type of tissue being chemosurgically excised, frozen sections may be used to determine the presence or absence of tuberculous involvement.

An advantage of the chemosurgical method is the fact that the tubercle bacilli are killed by the fixative while it is being used to remove the tuberculous lesion. Thus there is little likelihood of dissemination of the organisms during the procedure. After chemosurgical treatment the wounds are dressed with a cod liver oil ointment because of its inhibitory effect on tuberculous infection.

Certain lesions associated with other specific diseases such as syphilis and leprosy could, under special circumstances, be amenable to chemosurgical treatment but I have had no experience with them.

Sarcoid

Although the infectious origin of sarcoid is not definitely established the disease is considered here because in some cases at least, there seems to be an association with tuberculous or other infectious processes. Usually as in the four cases in the present series, the lesions do not contain viable organisms, possibly because they have been eliminated by the granulomatous process.

While the clinical manifestations of the cutaneous forms of sarcoid ordinarily are sufficiently characteristic to allow ready diagnosis there was some question of malignancy in each of the four patients who were chemosurgically treated. The tumors were removed mainly for the purpose of histologic diagnosis rather than for the purpose of therapy. Nevertheless all of the lesions were eradicated and never returned although one patient who had involvement of the parotid gland subsequently developed another sarcoid in the opposite parotid gland. Neither did any of the patients show roentgenographic evidence of tuberculosis or other infection.

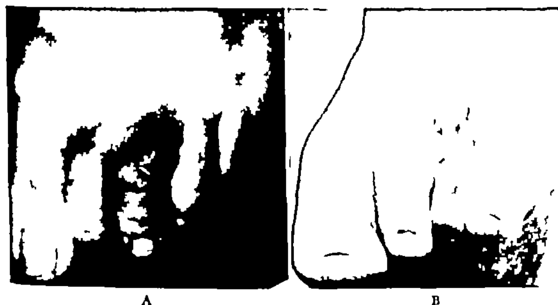


Fig. 220. (A) Tuberculous osteomyelitis which involved the proximal phalanges and the distal ends of the metatarsals of the third and fourth toes. (B) Healed lesion after chemosurgical amputation through the distal third of the metatarsals. There was no recurrence after nine years.

In general, chemosurgery is not recommended in the treatment of sarcoid unless the removal of the lesion is desired for the establishment of the histologic diagnosis or unless the disease is manifested by a single, well-defined nodule in a location where the resultant scar would be cosmetically satisfactory. Not infrequently the lesions disappear upon systemic treatment and they even may regress spontaneously.

Osteomyelitis

Osteomyelitis produced by pyogenic organisms may be amenable to chemosurgical treatment if the lesion is sufficiently accessible. For

example, in one case in which there was infected tibial bone in the base of a traumatic ulcer of a year's duration, the chemosurgical excision of the infected bone and adjacent tissues produced a healthy, granulating wound. Subsequent skin grafts were successful and the wound remained healed. In a second case of the same type, but of sixty years duration, the ulcer and infected bone were removed with ensuing partial healing by second intention. However in this case some of the bone failed to form a line of demarcation in the usual three or four weeks, probably because of the long duration of the process. Therefore, the fixed bone was left in place and though it kept the wound from healing completely the lesion was much improved.

As has been mentioned in the chapter on gangrene there were a number of cases in which osteomyelitis overshadowed the gangrenous changes in the soft tissues. Such digits were successfully amputated by means of the chemosurgical technic. In another case, that of a patient without either arteriosclerosis or diabetes, a toe was chemosurgically amputated for osteomyelitis of traumatic origin.

Tetanus

The possibility of using the chemosurgical technic for the removal of lesions harboring tetanus bacilli was demonstrated in one case. The patient was responding poorly to tetanus antitoxin when chemosurgical treatment of a varicose ulcer over the tibia was instituted because it was the only conceivable point of entry. The lesion had been traumatized by the thorns of a raspberry bush. In the course of the chemosurgical excision an unsuspected pus-filled tract was uncovered revealing the hidden source of the tetanus toxin. The patient then promptly recovered. In addition to the fact that the chemosurgical method provides a good means for eradicating the anaerobic tracts and spaces which harbor the tetanus bacilli, it also kills the organisms and, due to the fixation of the tissues, it promptly stops diffusion of the soluble toxin from the infected area.

In the case here cited the ulcer was treated solely by means of the chemosurgical technic. However preliminary surgical excision might serve to eradicate the focus of infection more rapidly in some cases. Needless to say, antitoxin therapy should continue until the patient has recovered.

Aphthous Ulcers

A simple means of quickly eliminating the soreness of the canker sores which characterize aphthous stomatitis is by the application of the zinc chloride fixative paste to the ulcer for two or three minutes. The chemical produces a brief stinging sensation following which the patient's discomfort disappears and the lesion usually heals promptly without further attention. Whether there is one lesion or several dozen as there occasionally may be, the technic is equally effective. The zinc chloride promptly eliminates the causative agent in the ulcers and reduces the likelihood of reinfection.

Peridental Ulcers and Granulomas

These lesions, which usually are the result of a combination of infection and some predisposing structural defect, often may be eradicated by chemosurgical technics. Sometimes it may be expedient to excise the lesion under local anesthesia and then to cauterize the surface with dichloracetic acid. If further penetration is desired the zinc cloride fixative may also be applied. If the lesion is small, cauterization with these chemicals alone may suffice. The chemicals should not be allowed to contact the teeth any more than necessary although no adverse effects have been noticed from such contact. The cauterized tissues separate spontaneously within a few days and the lesions usually heal rapidly. In order to prevent recurrence, other measures such as antibiotics to control the infection and the removal of initiating structural defects may be indicated.

Black Hairy Tongue

This is the rare condition in which black hair-like, hyperkeratotic projections several millimeters in length may cover the dorsum of the tongue. The disease usually is considered to be of fungous origin and it is reported to be more common since the advent of antibiotics which apparently upset the balance between bacteria and fungi allowing the latter to become ascend

ent. In two patients with this disease the condition was rapidly brought under control by light cauterization of the involved surface with dichloracetic acid Regardless of whether fungi yeasts or bacteria are of accidental or of causal significance these organisms are effectively destroyed by the chemical at the same time that the papillae are cauterized Several treatments may be necessary before the entire surface returns to normal The cauterization should be very superficial so that no scarring results Of course in cases in which oxytetracycline chlortetracycline or chloramphenicol are the apparent cause, the effect of the withdrawal of these drugs may be awaited before more active treatment is carried out

Palliative Treatment of Infected Inoperable Cancers

When inoperable cancers are rapidly growing they tend to outstrip their blood supply and form necrotic sloughs which become infected and extremely malodorous Some temporary relief may be obtained by the chemosurgical excision of the infected necrotic material along with as much of the viable neoplasm as is expedient This procedure has been used in several cases of breast carcinoma in a case of advanced mycosis fungoides in a case of myeloma of the sternum and in other inoperable cases with significant though temporary palliation

PART V

CHEMOSURGERY AS A SPECIALTY

CHAPTER 33

Why Chemosurgery Should Be Practiced as A Specialty

BECAUSE chemosurgery embraces a broad field and because its employment requires a considerable body of know-how and special skill, the method had best be practiced as a specialty

The broadness of the field of chemosurgery is indicated by the long table of contents of this book. Not only is the chemosurgeon concerned with cancers of the skin of the entire body including such special structures as the nose ears and eyelids, but he also is interested in orificial and cavitary cancers such as those of the lip mouth, nasal cavity sinuses larynx, penis, vulva, vagina anus and anal canal In addition, other neoplasms such as carcinoma of the parotid, melanoma, sarcoma and endothelioma of the various parts of the body are included in the field, not to mention benign tumors, precancerous lesions, gangrenous conditions and infections. Thus, no paucity of patients with diseases amenable to chemosurgical treatment is to be expected in any large center of population.

With regard to the specialized skill and know how required of a chemosurgeon, it is obvious that the very diversity of applications of the method presupposes a knowledge of broad scope. He must be unusually familiar with the anatomy of all of the areas in which he must work because he must predict just what structures the applied fixative is going to penetrate. He not only must know the expected natural history of the various types of neoplasms that he may encounter but he also must know their gross and microscopic pathology and their response to other forms of treatment. He must develop and maintain by constant practice a thorough familiarity with the factors which affect the penetration of the fixative chemical. He must acquire dexterity in the excision of the fixed tissues in order that the specimens will be intact and properly oriented. He must learn to differentiate by microscopic examination between cancer tissue and a variety of other structures that may have similar appearances. Even such a seemingly simple procedure as the application of a well fastened occlusive dressing requires some special technics, particularly in locations such as the lip and the eyelids.

Hence the practice of chemosurgery involves such a wide variety of information and special skills that specialization of some degree is necessary for the attainment of optimal results.

The degree of specialization may vary with the individual Thus, it is permissible to practice chemosurgery in connection with other specialties concerned with cancer For example, among my trainees have been dermatologists, plastic surgeons, general surgeons, general practitioners and cancer investigators. The important point is that for best results the chemosurgical method should be used intensively and regularly Cancer is too serious a disease to use any technic on a casual sporadic basis and this is particularly true of the chemosurgical technic. However for some of the conditions other than cancer the chemosurgical technics may be used safely without special training and experience.

Whether chemosurgery is practiced full time or in conjunction with some other specialty is something which may be left for the individual practitioner to decide. However in order to do the best work a certain amount of special training is necessary The period of training may

vary according to the previous training and experience. Dermatologists have the advantage of being able to differentiate clinically between cancer and a variety of other conditions which resemble cancer and usually they have a good knowledge of histopathology Surgeons have the advantage of familiarity with operative technics and usually are familiar with the behavior and appearance of the various neoplasms and most of the other diseases that come within the field of chemosurgery Such prior experience is very useful to anyone wishing to study chemosurgical technics, and it may allow the development of adequate skill in a relatively short time.

Persons having no previous special training require a more extended period of training in chemosurgery, preferably a year or more. At this time no specific period of training has been decided upon, but in the future it may be advisable to establish definite minimum standards of training

Another reason why chemosurgery should be practiced as a specialty is that a special clinical setup is required. An important part of this setup is the provision for the preparation of the special type of frozen sections needed to attain complete microscopic control of excision. The microtechnical facilities should be located within the clinic or at least in close proximity to it. The technician must be specially trained to handle the large specimens without the loss of any portion because any incompleteness could be the cause of failure to eradicate a cancer The proficiency that comes from experience also is important on the part of the assistants and nurses because they contribute to the smooth operation of the clinic and this in turn affects the thoroughness with which the meticulous technic is carried out.

A final reason why chemosurgery should be practiced as a specialty has to do with the personal attributes of the person who proposes to do chemosurgical work. Anyone who has had experience with chemosurgery realizes that the temperament of the operator could strongly affect the results obtained with the procedure. For example, a general surgeon who is accustomed to big sweeping incisions might well be temperamentally disinclined to carry out the multiple, careful excisions which characterize the chemosurgical technic. Similarly an individual who tends to shy away from tasks that require long periods of sustained effort might well be dismayed by some of the more advanced cancers that commonly come to the attention of the chemosurgeon. The quality of persistence is invaluable to a person planning to undertake chemosurgical work. Manual dexterity and good surgical judgement also are highly desirable qualities.

In summary chemosurgery should be practiced as a specialty for the following reasons (1) Chemosurgery embraces a broad field. (2) Special knowledge and skills requiring some degree of training are essential. (3) A special clinical setup is required. (4) The personal attributes of persistence, meticulousness, manual dexterity and good surgical judgment should be possessed or acquired by the persons who enter the field of chemosurgery

CHAPTER 34

Setting Up the Chemosurgery Clinic

THE facilities and personnel required for the practice of chemosurgery will vary with the size of the practice and the variety and extent of the lesions to be treated. Some details of the setup also depend upon whether the clinic is to be in a general hospital or in a private office. Since the chemosurgical method may be practiced to best advantage in a large general hospital I shall emphasize the setup which has worked out well in the Wisconsin General Hospital.

Floor Plan

The Chemosurgery Clinic at the Wisconsin General Hospital includes the following rooms (1) doctor's office (2) waiting room (3) operating room with small treatment chair (4) operating room with large treatment chair (5) operating room with operating table and (6) laboratory for microtechnical equipment and microscope (Fig 221). This arrangement has proved satisfactory except that the small waiting room and the lack of beds for patients who wish to lie down while waiting necessitates the use of adjacent rooms. The linear arrangement of the rooms was obligatory because of the design of the building but in structures with rooms in a more closely knit cluster it might be possible to devise an even more convenient plan. Regardless of the arrangement of the rooms the laboratory should be as close as possible to the operating rooms because of the considerable dependence of the method on frozen sections. It is desirable however that the laboratory have a door to separate it from the rest of the clinic because of the noise from the freezing microtome. The doors to the treatment rooms should be wide enough to admit wheel chairs and carts.

The doctor's office may have provision for a secretary's desk in the same room or preferably in an adjoining room. The records concerned with chemosurgical treatment are separate from the regular hospital records and they are kept in manila folders which are filed in steel cabinets in the office. A dictating machine facilitates the keeping of records on the progress of each case. A brief history the clinical and microscopic findings, the maps showing the progress of excision and other progress data are included in the charts.

The waiting room should be of a size proportional to the patient load expected. In a busy clinic the size of the waiting room illus

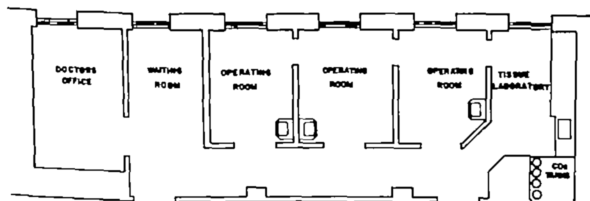


Fig 221 Floor plan of the Chemosurgery Clinic at Wisconsin General Hospital.

trated in Figure 221 is too small at times and often it is necessary to have patients wait in adjacent rooms. Crowding is undesirable in the waiting room because some of the patients may have advanced cancers which may be offensive to the esthetic sensibilities of some persons. Ordinarily a waiting room twice the size of that in the diagram should be planned for unless halls or adjacent rooms are available for the overflow

Three operating rooms are sufficient for one chemosurgeon and his staff At times more rooms would be useful but the extra distances necessitated by a larger clinic would tend to nullify the advantages. The rooms are inter connected to allow rapid movement from one patient to another

The first two rooms contain treatment chairs which can be placed in reclining positions. In the first room there is a small manually operated chair This is particularly convenient when patients with lesions in the mid-portion of the face are being treated because the patient's head may be lowered into the lap of the operator who sits at the head of the chair In the second room is an electrically operated treat ment chair (Ritter model MB) This is particularly useful when the operator wishes to stand while working The easy adjustment for height is helpful in getting the patient in a convenient working position, an important consideration when a long operation is being carried out.

The third operating room contains an elec trically operated operating table with a sponge rubber top (Ritter model B) This is necessary for non ambulatory patients and is convenient for many others, especially for those with lesions elsewhere than on the face. There should be enough leg room under the ends of the table to allow the operator to sit while working on lesions of the head or feet. The table should have stirrups for pelvic examinations and an arm rest for treatment of lesions of the arm and hands.

In each of the operating rooms are shelves and cabinets to allow convenient disposition of the instruments and supplies. In the middle room is a sterilizer for the instruments which are kept in this central location to allow convenient access from all rooms. Each room has a lavatory with knee-operated valves for hot and cold water Electrical jacks which hang from the ceiling provide current at six volts for the beam-type headlights. A telephone plug is connected to the cord of each headlight for ease in making a connection.

The laboratory is connected with the treat ment rooms to allow ready access for examina tion of the frozen sections. In the illustrated plan no door was provided and as a result the noise from the freezing microtome startles some patients and makes conversation difficult. One solution of this defect would be the installation of an easily operated swinging door and the use of sound absorbent material on the walls and ceiling Another solution would be the installa tion of a refrigeration unit to replace the carbon dioxide for freezing the sections.

The benches in the laboratory should be of desk height in order that the technician and the person using the microscope may sit in an unstrained position. Higher benches with high stools are usable but are less desirable. There should be storage space for microscope slides as well as for chemicals, stains and other materials used by the technician.

The tanks for the carbon dioxide which is used for the freezing microtome may be located in the laboratory or in an adjoining room, whichever allows most easy access. To reduce the likelihood of running out of carbon dioxide, four tanks are connected to the line leading to the freezing microtome Siphon tanks, type S.2 are most convenient since their squat shape makes them easy to handle. Moreover they may be used in an upright position whereas the long tanks should be horizontal.

The freezing microtome should be placed adjacent to the microscope so that the tech nician may place the completed microscopic slides next to the microscope without moving from her seat.

Instruments, Dressings and Solutions for the Operating Rooms

Each operating room has an instrument table with casters and with a rail around the back and sides. On these tables are placed the instruments and dressing materials that are regularly used in chemosurgical work (Fig 222) In-

cluded are forceps, scissors scalpels needle holder curets, and syringe in addition to dressing materials such as two-inch and four inch gauze flats cotton balls large and small cotton tip applicators, non-absorbent cotton tip applicators for applying the fixative and tongue blades. A petrie dish containing zinc chloride fixative impregnated gauze squares for use in stopping bleeders is placed within easy reach loss of zinc chloride solution by absorption into the wood For the same reason the applicators used to apply the fixative are wound with non absorbent cotton There is a large jar of clean but not necessarily sterile petrolatum which is used to spread on the second layer of cotton to make an occlusive dressing

The solutions most frequently used are along the rear rail of the treatment table The three



Fig 222. Instrument table with the usual setup

These "Z squares," as they are called, are made by spreading the zinc chloride fixative on fine meshed gauze leaving the meshes open. They are cut into squares varying from 1 to 10 millimeters across. They are kept on a piece of gauze soaked in a 40 per cent solution of zinc chloride to prevent drying and curling. Dichloracetic acid is kept in small amounts in a small, low bottle which will not tip easily The zinc chloride fixative is kept in a three-ounce jar The tongue blades used to dip out the fixative are impregnated with paraffin to prevent tables each have a bottle of cocaine hydrochloride but they are of different strengths 2 per cent for use in the eye, 4 per cent for mucous membranes and 10 per cent for ulcerated surfaces. The latter often is used to anesthetize nerves attached to the final layer of fixed tissue before they are cut. Sodium bicarbonate, in saturated solution (5.5 per cent) is left open so it is immediately available for neutralization of spilled or misapplied dichloracetic acid. Mercurochrome in 10 per cent solution is a much-used antiseptic. Hydrogen peroxide is

used to remove crusts exudates and blood it also is a mild antiseptic. Boric acid in saturated solution (4 per cent) is useful for wiping exudates out of eyes or from membranes and it is much used to moisten the cotton used to keep the surfaces of the wound moist while frozen sections are being awaited. Alcohol, in 70 per cent solution is used to clean the skin pre-

Pipe cleaners are stuck in the corks of the bottles of bluing and India ink.

A sterile towel covers the top of the treatment tables except where the bottles and jars are located. The instruments and dressings are kept sterile except for the handles of the instruments and applicators which are grasped with ungloved hands.

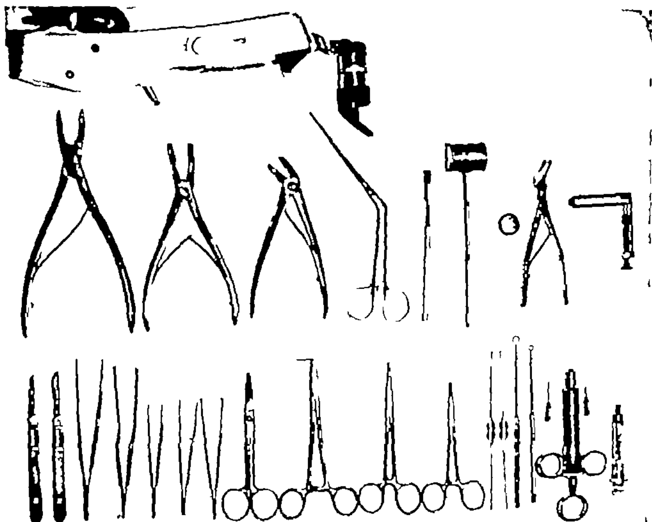


Fig 223 Recommended assortment of instruments. There should be six or eight of each of the much used instruments such as scalpels, forceps and scissors.

paratory to the injection of procaine. Benzine is used to remove tape marks and to remove the oil from the skin before applying adhesive tape.

Small bottles of mercurochrome, bluing and India ink for marking the edges of specimens are strapped to the side rail of each table where they may be reached easily A sharp-pointed, cotton-tip applicator is stuck in the cork of the bottle of mercurochrome which also is used to mark the origin of the specimens on the lesion.

In the drawers of the treatment tables are kept adhesive tape, bandage scissors, knife blades and other small items in frequent use. On a shelf below is the pad of paper on which maps of the lesion are drawn during excision of the specimens.

Less frequently used instruments are kept in adjacent sterile containers and in cabinets (Fig. 223) Besides the instruments mentioned above are rongeurs, special nasal forceps, chisels, mal-

lets aural nasal and vaginal speculae, probes, and hemostats The sterile instruments and dressing materials are kept in sterile containers on the window ledge shelves Headlights are hung on hooks adjacent to each treatment chair and operating table An electrosurgical unit such as the Bovie Model O 4 is kept in the operating room. Analgesia apparatus employing either nitrous oxide or trichlorethylene (Trimar Ohio Chemical Co) is available but is not often used As a rule general anesthesia is not employed in the Chemosurgery Clinic A suc

illustrated in Figure 224) Microtomes having a knife carrier held by multiple pivots tend to become loose with wear with the result that the knife may slide up over the specimen on one cut and then take a deep bite on the next The stage is modified to eliminate the back half which has openings for cooling the knife an unnecessary and expensive practice

The microtome the stains and other solutions are placed near a source of cold tap water and adjacent to the microscope (Fig 224)

The dyes dehydrating solutions, clearing

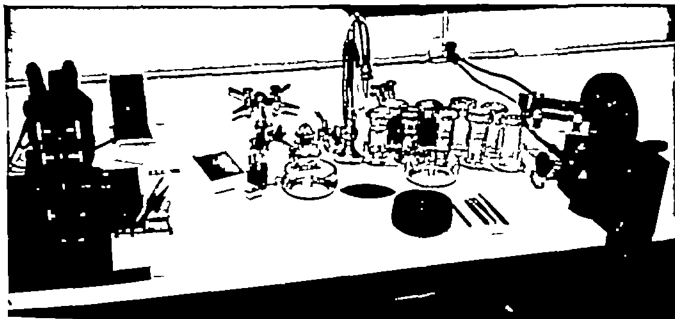


Fig 224 Setup for making frozen section in the Chemosurgery Clinic.

tion apparatus is available for use during treatment of intraoral lesions.

Equipment for the Laboratory

Because considerable time is spent each day scanning the frozen sections which are used to guide the chemosurgical excisions the microscope should be a binocular instrument of high quality The field of vision should be large. Most of the scanning is done with an ordinary lower power objective but low low high and oil immersion lenses also should be available A mechanical stage ordinarily is not used but is useful at times when the high power objective is being used

The freezing microtome should be a rugged instrument with a carriage that slides on tracks (for example, the Bausch and Lomb microtome

agents and other materials used in the preparation of the microscope slides are described along with the microtechnic in the following section which has been written with the help of Mrs. Eleanore Halvorson Sweitzer and Mr Robert Patnaude.

Microtechnic Used in Preparation of the Frozen Sections[44]

The complete microscopic control of excision which is afforded by the chemosurgical method is obtained by means of frozen sections which must be of unusually high quality Not only must the sections be well stained and well cleared but, above all, they must be complete. The preparation of such sections requires attention to a number of technical details which are included in the following description

Mounting the specimen on the microtome stage is done in such a way that a complete section is cut through the under side of the flat piece of tissue. Routinely the specimens are given to the technician lined up in their proper sequence on a gauze flat. The average specimen is a flat piece of tissue approximately 1 to 2 mm. thick and 1 cm. across. The under side of each specimen is placed downward and since it is the under side that is to be sectioned the first thing the technician does is to turn the specimen over. The under surface then is flattened by gently passing the broad surface of a smooth scalpel handle over it, and at the same time the specimen is oriented in the position in which it is to be placed on the stage.

It is important that the specimen be oriented so that the microtome knife strikes the narrowest part of the specimen first and moves diagonally over the large part of the specimen (Fig. 225A–D). Specimens containing muscle

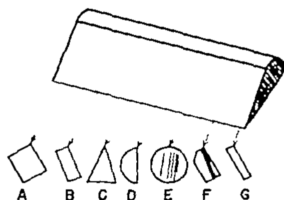


Fig. 225. Diagram showing optimum positions of specimens of various shapes and consistencies in relation to the microtome knife.

fibers or long strips of cartilage are oriented so that these structures are parallel to the direction of movement of the knife (Fig. 225E and F). If a vertical section of a flat specimen is to be cut, its long axis is placed at an angle of about 65° in relation to the knife (Fig. 225G). Unless the specimen is very small the specimen should not be placed so that the entire edge of the specimen meets the knife at the same time because this will crush the tissue, cause the knife to jump over the specimen or push the entire block off the stage. Specimens containing skin are placed so that the skin edge is cut along with the soft tissue to avoid crushing of the softer tissue. Tissues which are heterogeneous in consistency are placed so that the softer part is cut first. This provides a firm backing for the knife to cut against.

Three preparation dishes are filled with cold water ready for use. One dish is placed directly in front of the technician to receive the sections as they are cut. The cut sections are more easily seen if the inside of this dish is painted black. The dish is filled to the top with water to which a few drops of an aqueous solution of zephiran chloride, 1:1000, are added with a dropper to reduce the surface tension which otherwise may tend to break up the more delicate specimens.

The microtome stage is moistened slightly by rubbing a wet finger across it. The stage then is cooled until frosted by rapidly opening and closing the valve several times. With a medicine dropper, albumen solution is placed on the corner of the stage nearest the technician in an amount sufficient to accommodate the size of the specimen to be cut. Albumen solution is used instead of water not only because it freezes to ice that is less hard and brittle but also because it holds the specimen to the stage more firmly. Air bubbles in the albumen should be avoided because they cause depressions in the specimen.

The properly oriented specimen is deposited in the partially frozen ice making sure the under surface of the tissue is directed upward. The scalpel handle is kept on the specimen while the valve is again opened once or twice in order to freeze the tissue enough to hold it in position. Before the ice is frozen solid, any edges that are not level are raised by running the scalpel blade into the ice beneath that portion. This should not be done if the ice is solid because the edges might crack and chip away. A few drops of water may soften the ice enough to allow elevation of the edge but if it doesn't the tissue should be allowed to thaw before trying again.

When the specimen is level the tissue is frozen hard by opening and closing the valve several times with the left hand while the scalpel handle is kept moving over the tissue to keep it level. The specimen should be surrounded by ice as it is cut so that its edges are supported and protected.

Cutting the specimen ordinarily is done at a thickness of approximately 25 microns. However fragile tissues such as cancer tissues with meager connective tissue stroma, fatty tissues and tissues heavily infiltrated with leukocytes had better be cut at 30 microns. Tissues containing cartilage or considerable amounts of connective tissue are firm enough to allow cutting at less than 25 microns. Vertical cuts of specimens often may be cut as thin as 15 microns.

Using the coarse adjustment the stage is elevated slowly with the left hand while the knife is moved back and fourth with the right until the knife begins to cut the tissue. Then the automatic feed mechanism is locked in place and the specimen is cut with even complete turns of the wheel. The knife is stopped at the point of furthest forward advance. The cut section which clings to the knife is removed with a moist finger of the left hand and floated on the surface of the water in the dish in front of the technician. With a dry finger or towel the knife is wiped dry so that no water will fall on the specimen with the return stroke causing slight thawing with consequent thicker cutting on the next cut. Ordinarily four or five complete sections are cut from each specimen and placed in the same dish.

When there are several specimens waiting to be cut they should be kept moist with a small amount of water or albumen solution. After each specimen is cut, both sides of the knife should be wiped so that pieces of one specimen are not accidentally mixed with the sections of the next specimen.

It is extremely important that the knife be kept clean and very sharp. A dull or nicked knife may cause most of the difficulties encountered while cutting sections. It should be stropped daily and honed every week or ten days. The use of the knife at room temperature has been found satisfactory and it is not justifiable to waste the large amount of gas needed to freeze the knife.

Difficulties most frequently encountered while cutting are listed herewith along with the remedies. If the section rolls up tightly or splinters while cutting it has been frozen too hard. The specimen may be melted slightly by rubbing a dry finger across it after which the knife is passed across a little slower. The knife should not be allowed to stop midway across the specimen as this will cause slight thawing at that point with resulting deeper cutting through the remainder of the specimen.

If the tissue crumples like tissue paper against the edge of the knife the tissue is not frozen hard enough or has thawed too much. The tissue should be refrozen and the level of the knife readjusted.

If the section is very fragile and it breaks up despite the zephirin in the water it may help to dip the finger in zephirin rather than in water before removing the section from the knife. This facilitates the handling of fatty tissues also.

If part of the specimen is cut thicker than the rest or if the knife slips over the top instead of cutting and then on the next turn cuts too deeply it is because the knife is dull.

If the entire block is knocked from the stage the knife may be dull, the specimen may not be placed at the correct angle or the albumen solution may be too weak.

If the section after being cut swings back and clings to the stage it may not have been mounted close enough to the edge of the stage or the section has not been removed from the knife quickly enough.

Fixation of fresh tissues often is required because the first specimen taken from the patient usually is removed surgically and a vertical section is required immediately for diagnosis. To fix the fresh tissue it is placed in 10 per cent formalin and warmed slightly over an alcohol lamp. Before mounting on the stage the tissue is cut so that sections will be made through the center of the specimen along its longest axis. The tissue is held on edge with a splinter forceps and mounted on the stage at an angle of 65° in relation to the knife. It is not always necessary to fix the fresh tissues before cutting. However after cutting and mounting sections of fresh tissue on the slide the sections should not be blotted because they will stick to the towel. Instead the slide should be passed over an alcohol flame several times until dry. Overheating should be avoided because the tissue steam produced in this way has some

ıcy to fragment the tissues. With fresh ; the slide must be left in hematoxylin the usual time

unting the sections on the microscope slide ıe by working the tissues onto the slide ı curved metal teasing needle. If there is lency for the specimen to break up it is tant that all of the fragments be pieced .er so that no part of the section is missing dges of the specimens usually have been d with coloring materials (mercuro- ɛ, washing bluing and India ink) for the se of orientation when examined under icroscope. These markings may be useful : rearrangement of any fragments that ıave fallen out. Any folded areas may be nted by floating off that portion of the ɔen and remounting without detaching hole specimen. If the section is curled up *y be uncurled by* attaching one edge to de and drawing the slide out of the water to unroll it. If the section is not too : it frequently is possible to work the roll by gently moving it around in the water *he wire teaser*

he sections hold together well and there doubt of their completeness, it is unnec to mount more than one or two sections. ver if there is a chance that parts of of the sections may be missing more sec should be mounted on the slide. To save and cover glasses as well as to save ıng time it often is possible to mount four ıre sections of different specimens from me patient on one slide.

ɛr the sections have been mounted on the hey are blotted carefully and thoroughly ı very dry soft towel, preferably an old hat has the lint washed from it. It is ble to blot only one of the sections first if the section will cling to the towel. If s so the other sections may be fixed to the by passing it through an alcohol flame l times. The slide is numbered with a wax and put in 95 per cent alcohol to await ıg

ning is by a modified hemotoxylin-eosin d. The various solutions are kept in ı jars which have five slots that keep the apart. Care must be exercised to avoid putting two slides in one slot causing the sections to be rubbed off

There are two methods by which the slides may be passed through the various solutions. Either the slides may be left in the 95 per cent alcohol until five slides are ready to be stained or the first slide may be started through the staining process while the next specimen is freezing on the microtome. The latter method is preferred because it is quicker but some experience with the method is required in order to be able to keep track of the slides in the various stages of staining and at the same time to cut other sections. Except for the parlodion, acid alcohol and eosin the length of time in the solutions may vary considerably allowing considerable leeway for carrying out other parts of the procedure.

The steps in the dehydration staining, clearing and mounting of the sections are as follows

(1) *Ninety-five per cent alcohol* The slide may be left in this solution for any time over fifteen seconds.

(2) *Parlodion (purified pyroxylin)* The *slide is quickly dipped in this solution* which should be rather thin. If it is too thick, it and the sections tend to peel off the slide. Moreover a thick layer prevents the ready penetration of the stain and prolongs the process. If the solution is too thin or *if this step is omitted*, the sections tend to come off the slide. After dipping, the slide is blown gently until a film is formed and then it is blotted firmly with a clean dry towel.

(3) *Hematoxylin* Approximately one minute is the usual staining time but the slide may be left in longer if the tissue does not stain well. Delafield's hematoxylin is used. This stain lasts indefinitely but it is advisable to remove the precipitate every day before using by passing through filter paper After staining, the excess dye is washed off the slide in a dish of water

(4) *Acid alcohol* This solution is just strong enough to destain the average section in one dip. It is changed once a week or more often if necessary

(5) *Alkaline water* If the tap water is alkaline it is convenient to let the slide stand in a dish of water to alkalize. Otherwise a weak solution of sodium bicarbonate is used and the

sections are allowed to remain in the solution until they are blue. This usually takes one or two minutes. Only one slide should be in the solution at one time because the sections may loosen and come off at this time and be mixed. If a section floats off it may be mounted as before, blotted with a towel, and continued in the staining process. The sections should be blotted at this stage to insure removal of water and air bubbles from under the sections.

(6) *Eosin.* This solution is adjusted so that one dip of the section gives adequate staining. The stain may be diluted with 95 per cent alcohol if it stains too deeply. Alcohol also is needed to replace that lost by evaporation. The solution should be filtered whenever particulate matter gathers in it.

(7) *Alcohol and ether.* The sections are left in this solution for two minutes or more to remove the parlodion. The solution is made up of equal parts of ether and 95 per cent alcohol and it should be changed daily.

(8) *Absolute alcohol.* The sections are left in this solution for one or two minutes or until all of the parlodion has been removed. This solution should be changed once a week or more often if necessary for complete dehydration of the sections.

(9) *Carbol xylol.* The sections are left in this solution until the tissues are clear. Two minutes or more may be required. The solution ordinarily is changed once a week.

(10) *Xylol.* The sections are left in this solution for two minutes or more. The solution should be changed weekly.

(11) *Mounting in Permount.* This material is preferable to balsam because it hardens more rapidly and it does not turn yellow with age. Cover glasses of large size (22 × 50 mm.) usually are used in order that several sections may be placed on one slide.

If more speed is desired the staining process may be shortened by agitating the slides gently in each solution. When this is done the sections should be watched carefully and if they begin to loosen because of the agitation, they should be blotted gently with the dry towel and the staining continued. An experienced technician can process a dozen sections in less than a half hour.

Sections made with this technic have not deteriorated after periods of nearly twenty years.

The preparation of solutions generally is similar to that described in standard books on microtechnic such as that of Guyer.[24] However, since there are a number of modifications to suit the special technic, the various solutions and their preparations are given herewith.

(1) *Albumen solution*

Powdered albumen (Mallinckrodt)	0.2 gm.
Water	100.0 cc.
Phenol (saturated solution)	0.5 cc.

The latter is added as a preservative.

(2) *Parlodion stock solution*

Parlodion (purified pyroxylin, Mallinckrodt)	2 sticks
Ether and 95 per cent alcohol (equal parts)	60.0 cc.

Parlodion, diluted for use

Parlodion stock solution	20.0 cc.
Ether and 95 per cent alcohol (equal parts)	15.0 cc.

(3) *Hematoxylin (Delafield's modified)*

Hematoxylin crystals	4.0 gm.
Methyl alcohol	25.0 cc.
Aluminum ammonium sulfate, saturated solution	400.0 cc.

(Made by adding 77 gms. of aluminum ammonium sulfate crystals to 400 cc. distilled water and heating to dissolve.)

The hematoxylin dissolved in the methyl alcohol is added to the alum solution and exposed to light in an unstoppered bottle for 3 or more weeks. Then add

Glycerine	100.0 cc.
Methyl alcohol	100.0 cc.

This final solution is allowed to stand in the light until the color is sufficiently dark (deep wine-red color), usually three months. Then it is stored in a stoppered bottle in a dark cupboard until needed.

(4) *Acid alcohol*

Alcohol, 95 per cent	370.0 cc.
Water	130.0 cc.
Hydrochloric acid, concentrated C.P. (37 per cent)	25.0 cc.

(5) *Eosin alcoholic*

Eosin, water soluble	2.5 gm.
Water distilled	500.0 cc.
Hydrochloric acid concentrated (36.5 per cent)	4.0 cc.
Glacial acetic acid	1.0 cc.

The eosin is dissolved in water and the hydrochloric acid is added with a dropper. The precipitate which forms is allowed to settle and then the water is poured off and discarded. The precipitate is washed with water by decanting six times. The precipitate is filtered and dried on the filter paper in an oven at 52° C. for 24 hours.

Eosin stock solution

Precipitated eosin on the paper approximately	0.5 gm.
Alcohol, 95 per cent	100.0 cc.

Eosin diluted for use:

Eosin stock solution	5.0 cc.
Alcohol, 95 per cent	55.0 cc.
(6) *Carbol-xylol*	
Xylol	300.0 cc.
Phenol, pure melted crystals	100.0 cc.

Microtechnical equipment needed include the following:

- 10 Coplin jars with covers, for staining.
- Three preparation dishes, 11 cm. in diameter, 5 cm. deep.
- Microscope slides, 26 x 77 mm. (1 x 3 inches)
- Cover glasses, 22 x 50 mm.
- Curved metal teasing needle (dissecting needle with wood handle)
- Cover glass forceps with bent prongs.
- Splinter forceps (for holding vertical sections)
- Scalpel, Bard-Parker or ASR, with detachable blades.
  (*Discards from the operating rooms are satisfactory.*)
- Small dropper bottles for albumen solution, zephiran, and permount.
- Alcohol lamp.
- Filter paper and funnel.
- Small (5.0 cc.) beaker for heating formalin to fix fresh tissues.
- Red wax pencil.
- Freezing microtome as previously described. A refrigeration unit may be used instead.
- Microtome knives.
- Strop and hone.

Personnel of a Chemosurgery Clinic

In the Chemosurgery Clinic at the Wisconsin General Hospital there are, in addition to the chemosurgeon, the following personnel: (1) technician, half time; (2) combined technician and assistant; (3) nurse; and (4) secretary. This has been found to be the most economical arrangement for the type of work done in this clinic.

The regular technician works mornings when there is the heaviest load of microscopic work. The technician-assistant takes over the microtechnical work in the afternoons when the regular technician is absent. He also takes over when the technician is on vacation or absent because of illness. To afford extra assurance that facilities for frozen sections always will be available the nurse and secretary also are trained to make sections should both of the technicians be absent.

The technician's main work has been outlined in the section on microtechnic. However, besides making the frozen sections she keeps the microtome knives honed and stropped, she sees that a specimen for each patient is sent to the laboratory for a paraffin section, and she helps in the compilation of the results of treatment. In the absence of the nurse or of the secretary she takes over their work because besides being a technician she is a registered nurse and a proficient typist. When she is so occupied the technician-assistant takes over the microtechnical work.

The technician-assistant is a dexterous young man with training as a medical technician. He regularly assists the operator in many ways such as by providing retraction, holding bleeders, drawing maps of the lesion showing the origin of the specimens and completing most of the dressings after the fixative has been applied by the operator. As has been stated, in the absence of the regular technician, he takes over her duties in the laboratory. Likewise, in the absence of the nurse he takes over some of her duties. He also attends to sharpening the instruments, keeps track of the carbon dioxide supply and he helps carry out various research projects both in the clinic and in the laboratory.

The nurse sets up the treatment tables and tends to the sterilization and care of the instruments and dressings. She is responsible for getting the patients in the various operating rooms at the proper time. She usually removes the dressing, cleans the surrounding skin and, if necessary, clips the hair or shaves the area. She writes down the history and the results of the clinical examination. She sees that the needed instrument or medication is at hand at the proper moment. She writes prescriptions for analgesics and other drugs and presents them to the operator for inspection and signature. She keeps track of the nurses' notes on the hospital record and informs the operator of any unusual developments. She observes the reaction of the patient to treatment and if syncope appears imminent she lowers the patient's head, opens the window and administers spirits of ammonia. She often helps the operator by retraction, by holding bleeders, and by supplying instruments, drugs and dressing materials as needed. In addition she may draw maps showing the origin of the specimens.

Routinely she is responsible for the delivery of the specimens in proper order to the technician. She often applies dressings, especially after active chemosurgical treatment has been completed. She instructs the patients regarding dressings and the after-care of their lesions. She also makes a note of the date for a check-up visit and if the patient fails to return on the date set she has the secretary send out a form letter urging the patient to return. No member of the staff contributes more to make the clinic run smoothly than a well trained, efficient nurse.

The secretary also contributes a great deal to the smoothness with which the clinic runs. She not only calls the patients and attends to the many details essential to their efficient flow into the treatment rooms but she also answers the phone, makes room reservations for the patients, and takes them to the photographic studio when pictures are required. She types the case records and the letters to the referring physicians. She also enters each case in a compilation book under the appropriate headings according to the type of lesion.

The importance of selecting individuals who are well suited by training and by native ability for the various positions in the Chemosurgery Clinic cannot be too strongly stressed. An individual who is unable or unwilling to accomplish the duties which have been outlined can be worse than useless to the operator because such a person can upset the smooth running routine which is so important to the attainment of the best results with the meticulous chemosurgical technic.

The Future of Chemosurgery

Unless a specific cure for cancer is discovered the widespread use of the chemosurgical method seems inevitable. The greater use of chemosurgery will result from the increased demand for this treatment from physicians and from patients alike as they become aware of its unprecedented reliability, its conservatism, its low mortality rate and its other advantages. To supply this demand enough men must be trained in the use of the method to staff a chemosurgery clinic in each large center of population.

The development of facilities for chemosurgical treatment undoubtedly will be slow and gradual because the establishment of each clinic will have to await the decision of some individual to enter this new field. Inasmuch as the future of the field is largely uncharted it is unlikely that any but individuals with a flair for pioneering will be interested.

The manner in which clinics are set up will depend on the individual who elects to enter the field. Some will prefer to practice the method in conjunction with another specialty such as surgery, plastic surgery or dermatology, while others may wish to practice chemosurgery almost exclusively. As a result of this diversity of interests the scope of the practice in different clinics is likely to vary. Thus, individuals associated with dermatology clinics probably will largely limit their chemosurgical practice to the less advanced cutaneous cancers and to the other disease conditions that are likely to come to the attention of a dermatologist. Individuals whose training is in some surgical specialty and individuals who elect to practice chemosurgery exclusively probably will accept patients with any of the diseases taken up in this book including advanced cancers of the skin and other accessible structures.

I believe it is desirable that the chemosurgical method be taken up by individuals with varied backgrounds because each is potentially capable of bringing new knowledge and skills to the field. There is every reason to believe that the chemosurgical method will be further improved and that the indications for its use will constantly be revised. The more knowledge and know-how that are brought to bear on the problem the more the progress to be expected.

As I have said, most of the spread of the use of chemosurgery will depend upon individuals who elect to take the trouble to learn the technic. Probably most of these men will be relatively young. Older men who are well established in their own field probably will not be inclined to exert themselves to the extent necessary to learn the new skills involved.

Whether the initiative to start a chemosurgery clinic comes from an individual desirous of entering this field or whether it comes from

an institution desirous of making provisions for such a clinic may vary with the particular situation. In the cases of most of my trainees the individual has expressed interest in learning the technic and the institution in which he worked has cooperated in helping the individual obtain the necessary training and facilities. It is to be hoped that many of the larger teaching institutions eventually will follow this example.

There is no reason why young men should not independently obtain training in the field of chemosurgery upon completion of their internships or residencies. Once they had mastered the technic they would have the choice of entering private practice, participating in group practice or practicing in a teaching institution. Large sections of the country which are lacking chemosurgeons should offer ample opportunities for well trained individuals.

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By

FREDERIC E. MOHS B.Sc., M.D

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